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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 04/38/03. The contractual start date was in July 2005. The draft report began editorial review in December 2006 and was accepted for publication in March 2008. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

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Objectives: To determine the clinical effectiveness and cost utility of procedures alternative to TURP (transurethral resection of the prostate) for benign prostatic enlargement (BPE) unresponsive to expectant, non-surgical treatments.
Data sources: Electronic searches of 13 databases to identify relevant randomised controlled trials (RCTs).
Review methods: Two reviewers independently assessed study quality and extracted data. The International Prostate Symptom Score/American Urological Association (IPSS/AUA) symptom score was the primary outcome; others included quality of life, peak urine flow rate and adverse effects. Cost-effectiveness was assessed using a Markov model reflecting likely care pathways.
Results: 156 reports describing 88 RCTs were included. Most had fewer than 100 participants (range 12–234). TURP provided consistent, high-level, long-term symptomatic improvement. Minimally invasive procedures resulted in less marked improvement. Ablative procedures gave improvements equivalent to TURP. Holmium laser enucleation of the prostate (HoLEP) additionally resulted in greater improvement in flow rate. HoLEP is unique amongst the newer technologies in offering an advantage in urodynamic outcomes over TURP, although long-term follow-up data are lacking. Severe blood loss was more common following TURP. Rates of incontinence were similar across all interventions other than transurethral needle ablation (TUNA) and laser coagulation, for which lower rates were reported. Acute retention and reoperation were commoner with newer technologies, especially minimally invasive interventions. The economic model suggested that minimally invasive procedures were unlikely to be cost-effective compared with TURP. Transurethral vaporisation of the prostate (TUVP) was both less costly and less effective than TURP. HoLEP was estimated to be more cost-effective than a single TURP but less effective than a strategy involving repeat TURP if necessary. The base-case analysis suggested an 80% chance that TUVP, followed by HoLEP if required, would be cost-effective at a threshold of £20,000 per quality-adjusted life-year. At a £50,000 threshold, TUVP, followed by TURP as required, would be cost-effective, although considerable uncertainty surrounds this finding. The main limitations are the quantity and quality of the data available, in the context of multiple comparisons.
Conclusions: In the absence of strong evidence in favour of newer methods, the standard – TURP – remains both clinically effective and cost-effective. There is a need for further research to establish (i) how many years of medical treatment are necessary to offset the cost of treatment with a minimally invasive or ablative intervention; (ii) more cost-effective alternatives to TURP; and (iii) strategies to improve outcomes after TURP.

Contents

List of abbreviations

AUA	American Urological Association
AUR	acute urinary retention
BNC	bladder neck contracture or urethral stricture
BPE	benign prostatic enlargement
B-TURP	bipolar transurethral resection of the prostate
B-TUVP	bipolar transurethral vaporisation of the prostate
B-TUVRP	bipolar transurethral vaporesection of the prostate
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CUA	cost-utility analysis
DAM	decision-analytic model
ED	erectile dysfunction
EQ-5D	EuroQol Five Dimensions
EVPI	expected value of perfect information
EVPPI	expected value of partial perfect information
HoLEP	holmium laser enucleation of the prostate
HIFU	high-intensity focused ultrasound
HRG	Healthcare Resource Group
ICER	incremental cost-effectiveness ratio
ILC	interstitial laser coagulation
ILD	individual level data
IPSS	International Prostate Symptom Score
KTP	potassium-titanyl-phosphate
LOS	length of stay
LUTS	lower urinary tract symptoms
MI	myocardial infarction
MTOPS	medical therapy of prostatic symptoms
NICE	National Institute for Health and Clinical Excellence
OPCS	Office for Population Censuses and Surveys
PSA	prostate-specific antigen
QALYs	quality-adjusted life-years
RCT	randomised controlled trial
RR	relative risk
SF-36	Medical Outcomes Study 36-item Short Form Health Study
TEAP	transurethral ethanol ablation of the prostate
TUIP	transurethral incision of the prostate
TUMT	transurethral microwave thermotherapy
TUNA	transurethral needle ablation

continued

TUR	transurethral resection	UTI	urinary tract infection
TURP	transurethral resection of the prostate	VLAP	visual laser ablation of the prostate
TUVP	transurethral vaporisation of the prostate	VOI	value of information
TUVRP	transurethral vaporesection of the prostate	WIT	water-induced thermotherapy
		WMD	weighted mean difference

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS) or it has been used only once or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Benign prostatic enlargement (BPE) commonly causes older men to have difficulty passing urine. If non-surgical management does not alleviate symptoms satisfactorily, the standard treatment is transurethral resection of the prostate (TURP). TURP requires an anaesthetic and a stay in hospital and sometimes has unwanted effects. Consequently, newer procedures using alternative energy sources have been developed. Some do not require a general anaesthetic, are carried out in outpatient settings and have fewer adverse effects. However, there is uncertainty about their clinical effectiveness and cost-effectiveness. This review aimed to:

- determine the clinical effectiveness of alternative procedures
- model estimates of cost and cost utility
- rank the clinical effectiveness and risk profile of newer procedures in terms of benefits, risks and cost-effectiveness
- identify areas for future research.

Description of proposed interventions

Surgery for BPE can be divided into 'minimally invasive' and 'tissue ablative' treatments. Minimally invasive procedures include transurethral microwave therapy (TUMT), transurethral needle ablation (TUNA), transurethral ethanol ablation of the prostate (TEAP) and transurethral laser coagulation. Tissue ablative procedures are as invasive as TURP and include laser prostatectomy, laser vaporisation, transurethral vaporisation of the prostate (TUVP), transurethral vaporesection of the prostate (TUVRP), and bipolar TURP, TUVP and TUVRP. Although the ablative techniques are grouped together for the purposes of this review, there are differences in the method of ablation of the prostate with some techniques using vaporisation (e.g. TUVP) compared with those using resection [e.g. holmium laser enucleation of the prostate (HoLEP)].

Methods

Clinical effectiveness

Electronic searches of 13 databases were conducted to identify randomised controlled trials (RCTs) of surgical interventions for BPE. Selected conference proceedings were hand searched, websites consulted and reference lists scanned.

Two reviewers independently assessed study quality and extracted data. The International Prostate Symptom Score/American Urological Association (IPSS/AUA) symptom score was the primary outcome; other outcomes included quality of life, peak urine flow rate and adverse effects.

Cost-effectiveness

A Markov model was produced reflecting likely care pathways. Parameter estimates were derived from the systematic review of clinical effectiveness, a review of previous economic evaluations and other UK relevant sources.

Results

A total of 156 reports describing 88 RCTs were included. The majority had fewer than 100 participants (range 12–234).

TURP provided a consistent, high level of long-term symptom improvement. Improvements in quality of life and flow rate were also observed. Minimally invasive procedures result in less improvement in symptoms and flow rate. Ablative procedures give similar symptom and quality of life improvements to TURP. HoLEP additionally resulted in greater improvement in flow rate. In terms of effectiveness, HoLEP appears to be unique amongst the newer technologies in offering an advantage over TURP, currently confined to urodynamic outcomes, which may not be of importance to patients, although long-term follow-up data are lacking. Severe blood loss was more common following TURP. The rate of incontinence was similar across all interventions other than for

TUNA and laser coagulation, which reported lower rates. Acute retention and need for reoperation was more common with newer technologies, especially the minimally invasive interventions.

The economic model suggested that minimally invasive procedures (represented by TUMT) were unlikely to be considered cost-effective compared with TURP. Strategies involving TUMT with TURP as a second procedure as necessary were more costly but had a similar effectiveness to TURP. Of the other ablative procedures, TUVP was less costly than TURP (and also the least costly single treatment considered) but less effective. HoLEP was estimated to be more effective and less costly than a single TURP but less effective than a strategy involving repeating TURP if necessary. However, the base-case analysis suggested an 80% chance that a strategy of TUVP, followed by HoLEP if required, would be the cost-effective strategy at a threshold of £20,000 per quality-adjusted life-year (QALY). At an approximately £50,000 threshold, on average, TUVP, followed by TURP as required, would be cost-effective, although considerable uncertainty surrounds this finding.

Sensitivity analyses

All changes found in the sensitivity analyses were intuitively sensible and their possible impact depended on society's willingness to pay for a QALY.

Limitations of the calculations (assumptions made)

The main limitations relate to the quantity and quality of the data available, in the context of multiple comparisons. Many trials were under-reported or poorly reported; much of the information available was in a form that was unsuitable for meta-analysis. Obtaining cost estimates was not always straightforward and costing under all resource categories was not possible.

Conclusions

For the NHS, increased use of TUVP and/or HoLEP would lead to an increased requirement for training, which may be costly; in addition, it would take time to establish an adequate level of provision. In the absence of strong evidence in favour of newer methods, TURP remains both clinically effective and cost-effective. The use of minimally invasive technologies in the NHS is not appropriate until a more effective and/or less costly technology is available.

Need for further research

1. For men who might currently be managed medically, a systematic review including modelling to determine how many years of medical treatment are necessary to offset the cost of treatment with a minimally invasive or ablative intervention in the first instance.
2. Better research into the true costs of the different interventions as a critical driver of economic evaluations.
3. Consensus work in partnership with governing bodies such as the British Association of Urological Surgeons to agree parameters for conducting future trials, such as standardising definitions and reporting of outcome measures.
4. For men judged to need ablative therapy, is there an alternative to TURP that is more effective, safe or cost-effective? A well-conducted head-to-head trial of treatment strategies – TUVP followed by either TURP or HoLEP, versus HoLEP, versus TURP × 2 – would be the most desirable to establish the gold standard. Such a trial should take prostate size into account and should include direct measures of utility. Newer technologies could then be compared against this gold standard and, given the rapid developments in this area, a tracker trial approach may be appropriate.
5. Trials of different strategies aimed at improving outcomes and minimising adverse effects after TURP, particularly bleeding.

Chapter 1

Aim of the review

The aim of the planned research is to assess the relative clinical effectiveness and cost utility of established and emerging interventional treatments for men suffering symptoms or complications caused by benign prostatic enlargement (BPE).

The specific objectives are:

1. To determine the clinical effectiveness of alternative procedures.
2. To determine the magnitude of risk of their short- and long-term side effects.
3. To rank the clinical effectiveness and risk profile of new interventional procedures against transurethral resection of the prostate (TURP), currently considered the gold standard of care.
4. To estimate the cost utility of the alternative procedures.
5. To assess the effects of skill and learning on cost-effectiveness.
6. To identify clinical indications and contraindications for specific procedures.
7. To assess the speed of development in the field.
8. To identify areas in which future research is required.

The research was based on four inter-related components:

1. Development of care pathways for the chosen treatment options for men presenting with symptoms or complications resulting from BPE.
2. A systematic review of the literature of the effects of the alternative procedures.
3. A systematic review of economic evaluations to inform (4) below.
4. Construction of a Markov model and cost-utility analysis of the treatment options.

Chapter 2
Background

Description of the underlying health problem

Introduction

Clinical BPE describes a condition affecting older men characterised by the combination of increased prostate size and urinary symptoms such as frequency and poor urinary flow that bother the patient. The pathophysiology of benign enlargement involves hyperplasia of the epithelial and stromal components of the prostate gland leading to progressive obstruction of urine flow, and increased activity of the bladder (detrusor) muscle. These secondary urodynamic changes of bladder outlet obstruction and detrusor dysfunction are thought to result in the typical bladder storage symptoms such as frequency and nocturia and voiding symptoms such as poor flow and intermittent stream. For simplicity, the variety of symptomatic effects are grouped together as lower urinary tract symptoms (LUTS). Although the precise relationship between symptoms, prostate enlargement and detrusor dysfunction can be debated, there is no doubt that removal of prostatic tissue in affected men results in improvement of symptoms, urodynamic parameters and quality of life.

Men are diagnosed as suffering from clinical BPE by documenting a combination of storage and voiding symptoms, finding a uniformly enlarged prostate gland on digital rectal examination and the measurement of a reduced peak urinary flow rate (Q_{max}). Q_{max} is normally used to predict response to surgery and acts as a proxy for urodynamic studies. Men with a Q_{max} of less than 10 ml/s are more likely to have urodynamically proven bladder outflow obstruction and as a result are more likely to have a good outcome after surgery. The usefulness of other indicators of lower urinary tract function, in particular the diagnosis of bladder outlet obstruction by invasive pressure flow studies, continues to be debated. In general, such testing before surgery will reduce the number of men having a poor outcome at the expense of denying a proportion of men classified as not obstructed successful surgery. Because Q_{max} was the only urodynamic inclusion criterion for the studies included in the systematic review, the utility of further testing has not been considered further.[1]

The diagnosis also requires exclusion of other lower urinary tract disorders by urinalysis, prostate-specific antigen (PSA) level and use of a frequency/volume chart. The severity of the disorder is assessed using a validated symptom-scoring questionnaire, most commonly the International Prostate Symptom Score (IPSS).[2] This questionnaire asks the patient to rate voiding symptoms (poor stream, intermittent flow, incomplete emptying, straining) and storage symptoms (urgency, frequency, nocturia) on a scale from 0 (none) to 5 (very severe). Completion of the IPSS yields a total score ranging from 0 to 35 defining mild (score 0–7), moderate (score 8–19) and severe (score 20–35) symptomatic states. In addition, a single disease-specific quality of life question scores how bothersome symptoms are for each individual [range 0 (delighted) to 6 (terrible)]. This basic assessment is used to discuss management options with each patient, which may involve lifestyle changes alone, drug treatment or invasive therapy to remove or ablate prostate tissue. In some men the predominant clinical problem is characterised as a complication of BPE. This can be recurrent lower urinary tract infection (UTI), bleeding (haematuria) or urinary retention. Such complications are generally an indication for invasive treatment to remove prostate tissue. Other assessment instruments include the well-validated American Urological Association (AUA) symptom index, which uses seven questions that are identical to the IPSS questions with the exception of the disease-specific quality of life question, and the Madsen–Iversen index, which is no longer recommended for assessing symptoms as it was not designed to be self-administered by patients. The Madsen–Iversen index is usually completed by an interviewer and includes questions about stream, straining to void, hesitancy, intermittency, bladder emptying, incontinence, urgency, nocturia and frequency, with different symptoms attracting different scoring schemes. Although providing semi-objective symptom quantification, these questionnaires, including the currently favoured IPSS, have been criticised for giving undue

weight to voiding symptoms at the expense of the sometimes more troublesome storage complaints.

Epidemiology and natural history

Clinical BPE is a common disorder, affecting 30% of those older than 60 years and 40% of those older than 70 years.[3] What is becoming increasingly clear is the generally progressive nature of BPE.[4,5] In a randomised comparison with TURP, 30% of men assigned to advice alone required prostate surgery for progressive symptoms during a 3-year period of surveillance.[6] Longitudinal community observational studies such as that performed in Olmsted County, USA[7] have shown an increase in both symptom severity and adverse effects on quality of life associated with progressive prostate enlargement and deterioration in urine flow. This study followed 2115 randomly selected white male residents and found that 26% of men aged from 40 to 49 years and 46% of men aged from 70 to 79 years reported moderate to severe urinary symptoms. Longitudinal data also confirmed an annual increase in prostate volume of 1.6%, an overall annual increase in symptom score of 0.29[8] and a consistent annual decline in peak flow of 2% across all age groups.[9] In the same cohort of patients there was an increased risk of acute urinary retention with increasing age, with baseline age, symptom severity, prostate size and maximum flow rate identified as independent predictors.[10] A potential drawback of such community-based studies is the lack of histological confirmation of benign hyperplasia, which in other studies has been found to be present in 40% of men in their 50s and around 90% of men in their 80s.[11–13] Although the natural history of clinical BPE is more accurately determined using community-based cohorts such as in the Olmsted County study, further insights are gained from placebo arms of trials of drugs used to treat clinical BPE, such as the medical therapy of prostatic symptoms (MTOPS) study[14] which documented that the risk of BPE progression averaged 17% at 4 years.

Significance in terms of ill health

The combination of improved life expectancy and reduction in birth rate has resulted in an actual or predicted progressive ageing of the population in most communities worldwide. For men, it is estimated that the population of those aged over 65 years reached 207 million in 2005, constituting 6.38% of the world's male population.[15] These demographic changes inevitably result in an increased prevalence of chronic health problems associated with ageing. This has been shown for clinical BPE by a number of epidemiological studies.[16] The prevalence of moderate to severe symptoms progressively increases from 18% of men in their 40s to 56% of those in their 70s.[17] The bothersome nature of urinary symptoms is linked to adverse changes in quality of life and drives men to seek medical advice and treatment. In the past the range of treatment was limited to open or endoscopic removal of the prostate but now options include single or combination drug therapy, phytotherapy and the application of various energy sources to remove or ablate prostate tissue. The increased range of therapies has encouraged more men to seek help to alleviate their symptoms and has led to a widening of the indications for interventional treatments. Thus, although it is rarely a life-threatening problem, clinical BPE represents a major and increasing health condition that consumes a significant proportion of health-care expenditure.[18]

The goals of treatment of clinical BPE are to reduce the severity of symptoms together with the bother that they cause, to normalise the dynamics of the lower urinary tract and to resolve or prevent complications. Treatment options balance likely benefits with possible occurrence and severity of side effects. Simple reassurance and lifestyle advice can be sufficient for those men without much bother but they incur the risk of later complications. Drug treatment can be effective for relief of symptoms and evidence suggests that long-term treatment with a drug combination may also lessen the risk of complications.[19] Drug treatment is, however, costly, of only moderate effectiveness and does not improve urodynamic status. Procedures that reduce prostate bulk combine higher effectiveness with the attraction of a single treatment, but they are associated with increasing severity of unwanted effects; open removal of the prostate (prostatectomy), for example, has the greatest effectiveness but results in the highest morbidity. Although still an option for larger glands, open prostatectomy is not commonly used for the treatment of BPE in the UK and will not be considered further in this review, which concentrates on newer interventions. TURP has been the mainstay of treatment for clinical BPE for many years because it combines high effectiveness with a previously acceptable side-effect profile. More recently, in the UK, men have tended to seek help earlier in the natural history of the disease and access to secondary health care has improved. This, together with increasing co-morbidities present in the ageing

population at risk and the desire of health providers to contain costs, has fuelled the search for less morbid invasive treatments. There is also some evidence that men without complications or severe symptoms would prefer a less morbid method of prostate ablation with a shorter hospital stay.[20] Technological developments have allowed clinical investigators and medical device manufacturers to apply alternative energy sources with varying degrees of invasiveness to achieve reduction of prostate bulk without some of the side effects of TURP, such as bleeding, cardiovascular disturbance due to irrigation, incontinence and ejaculatory dysfunction. These interventions can be subdivided into surgical procedures that generally involve removal of prostate tissue requiring general or regional anaesthesia and minimally invasive options, which do not require general anaesthesia and can be carried out in an outpatient setting.[21] The former group are generally more efficacious than the latter group but have higher complication rates; however, estimates of beneficial and unwanted effects do vary between procedures within these two categories.[21]

Description of new interventions

In this section we describe standard and newer interventions that will be compared in the review of clinical effectiveness and economic model. The UK government-funded health service (NHS) is fortunate in having comprehensive centralised data collection systems from which numbers of procedures and their costs can be extracted.[22] Unfortunately, current coding systems do not differentiate between energy sources used in prostate ablation, with all procedures coded as TURP. This makes it difficult to estimate the number of newer interventions being performed, and the occurrence rates for specific procedures given below should be considered as approximate. Considering the relevant OPCS-4 codes (M65.1, M65.2, M65.3, M65.8, M65.9, M66.2, M66.8, M66.9, M67.8, M67.9, M70.8), a total of 28,799 procedures were performed within NHS hospitals in England during the financial year 2004–2005 (main operation four-character codes 2004–2005), which tallies well with the count of 30,387 using the simplified Healthcare Resource Group codes L27, L28 and L29 (Healthcare Resource Group codes 2004–2005).[22] Given a total population of 49 million and a population at risk (men > 59 years) of 4.5 million, this gives crude incidence rates of 60 per 100,000 per year and 667 per 100,000 per year respectively for surgical treatment of clinical BPE.[23] *Table 1* provides a summary of the main surgical procedures, detailing the main characteristics, number of operations performed by the NHS in 2006 and cost.

Minimally invasive treatments

Introduction

Minimally invasive treatments seek to ablate BPE using low-energy heating devices. Typically temperatures of 40–80°C are achieved, causing areas of coagulative necrosis, which either slough via the urethra or are reabsorbed during tissue repair. The resultant defect is usually visible on transrectal ultrasound scanning but is considerably smaller than for TURP. Provided energy delivery is kept low these treatments can be carried out in the office or outpatient clinic, whereas higher energy levels require anaesthesia and hence an operating theatre. Delayed necrosis means that relatively prolonged catheterisation is required to avoid urinary retention and painful micturition and, as a consequence, treatment benefit may not be realised for 2–3 months.[24] The use of urethral stents is also discussed in this section.

Interventions

Transurethral microwave thermotherapy

Microwave energy is used in transurethral microwave thermotherapy (TUMT), achieving temperatures of 45–70°C in the prostate depending on the device and power setting. Initially, energy was delivered at low power settings but variable higher energy delivery is now more usual. Microwaves induce oscillation of water molecules causing heat generation and inducing coagulative necrosis of prostatic tissue.[25] The procedure is typically performed using an antenna mounted within a transurethral catheter through which cooling fluid circulates. Temperature control is regulated by urethral and rectal thermometer probes to prevent collateral damage. The procedure lasts for 30–60 minutes and is performed using local anaesthesia and oral analgesia together with sedation for high-energy protocols. Requirement for postoperative catheterisation varies from 1 to 12 weeks depending on the protocol used.[26]

Transurethral needle ablation of the prostate

Transurethral needle ablation (TUNA) of the prostate involves the delivery of radio frequency energy via a modified urethral catheter attached to

TABLE 1 *Comparative characteristics of main surgical treatment options for clinical BPE*

Procedure	Hospital stay	Energy source	Method of tissue removal	Period of catheterisation	NHS procedures (per year)[a]	Cost (£)[b]
Minimally invasive						
TUMT	Day case	Microwave	Coagulative necrosis	1–2 weeks	300	1800
TUNA	Day case	Radio frequency	Coagulative necrosis	3 days	100	1600
HIFU	Day case	Ultrasound	Coagulative necrosis	2 weeks	100	1000
Laser coagulation	1–2 days	Laser	Coagulative necrosis	3–7 days	500	750
Ablative						
TUIP	1–2 days	Diathermy	None	1–2 days	2500	1800
TURP	3–5 days	Diathermy	Resection	1–3 days	20,000	2000
Laser vaporisation	1–2 days	Laser	Vaporisation	1–2 days	3000	2600
TUVP	2–3 days	Diathermy	Vaporisation	1–2 days	2000	1800
HoLEP	2–3 days	Laser	Enucleation	1–2 days	1500	1900

HIFU, high-intensity focused ultrasound ; HoLEP, holmium laser enucleation of the prostate ; TUIP, transurethral incision of the prostate; TUMT, transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate; TUVP, transurethral vaporisation of the prostate.
a Estimated from a total of 30,000 procedures from hospital episode statistics data (NHS Health and Social Care Information Centre, 2006).[22]
b Estimated from NHS and manufacturer cost data.

a generator to ablate prostate tissue. Two adjustable needles located at the end of the catheter are inserted into the prostate under endoscopic control. The radio frequency waves generate ionic agitation of molecules within the prostate, which in turn produces a localised heating effect of up to 115°C resulting in areas of coagulative necrosis. Teflon sheaths are advanced over the needles following placement to a depth of 5–6 mm to protect the urethra. The radio frequency power is usually delivered at 2–15 W for 5 minutes per lesion.[27] Once the coagulative effect has been achieved the needles are placed in a different area of the prostate and the procedure repeated. Depending on prostate size, the procedure generally lasts between 30 and 60 minutes and is performed under local or regional anaesthesia.[28] An indwelling catheter is placed for up to 3 days and antibiotic therapy given.[29]

Urethral stent

The rationale for stenting of the prostatic urethra in men with BPE is to nullify the compressive and constrictive obstructive effect of the adenomatous tissue and hence reduce the bladder pressure required to open the urethra.[30] The currently available device is made of woven braided wire mesh that can be delivered and expanded in the prostatic urethra under endoscopic or radiological control. The proximal end is engaged in the bladder neck and the distal end must lie above the external sphincter to prevent incontinence. The procedure can be accomplished using local anaesthesia. The inner aspect of the stent becomes lined with epithelium over a 3- to 12-week period. Unfortunately, device migration, ingrowth of fibrous stroma and encrustation are common longer-term sequelae leading to explantation in up to 50% of cases.

High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) uses ultrasound as the energy source, which, when tightly focused, can cause coagulative necrosis of tissue. It is delivered by a transrectal probe equipped with a transducer incorporating both imaging and ablative capabilities on the same ceramic crystal operating at 4 MHz. Ultrasound can be delivered to a precisely located focal zone of 2×10 mm leading to a rapid rise in temperature of up to 80–100°C using short exposure duration. Multiple lesions are then created throughout the prostate by moving the probe, with a treatment session lasting about 60 minutes. A catheter is placed to drain the bladder throughout the procedure and remains in place for about 2 weeks.[31,32] The high temperatures achieved necessitate general anaesthesia or sedoanalgesia with the procedure carried out as a day case.

Transurethral ethanol ablation of the prostate

Transurethral ethanol ablation of the prostate (TEAP) is chemical ablation of prostatic tissue using dehydrated ethanol. This results in the development of intraprostatic necrotic areas due to dehydration, protein degeneration and thrombotic closure of arterioles and venules.[33] Delivery of absolute ethanol into the prostate can be achieved by injection via a transperineal,[34] transrectal[35] or transurethral[36] route. The transurethral route is the most commonly reported delivery route. Commercially available 0.5–2.0 ml injection of ethanol (99.5% v/v) is injected into the prostate using either an injection and aspiration set for periurethral injection (Richard Wolf GmbH, Knittlingen, Germany) or a cystourethroscopy injection system (Olympus Winter & Ibe GmbH, Hamburg, Germany). The sites of injection are about halfway between the bladder neck and the verumontanum at the 2, 4, 8 and 10 o'clock positions, at least 1.5 cm proximal to the external sphincter. The number of injections depends upon the size of the prostate gland. The requirement for postoperative catheterisation is longer than in standard TURP and the retreatment rates are higher.[37] There are no long-term outcome or cost-effectiveness reports.

Water-induced thermotherapy

Water-induced thermotherapy (WIT) destroys prostate tissue by way of heat energy delivered by hot water flowing through a urethral catheter made up of four contiguous sections – a urine drainage lumen, a positioning balloon, a treatment balloon and an insulated shaft.[38] The catheter is inserted into the urinary bladder and secured by inflating the positioning balloon. Hot water circulates through the treatment balloon, which lies in the prostatic urethra, and is precisely maintained at 60°C (140°F) by thermocouples located in the catheter and machine. The procedure takes approximately 45 minutes under local anaesthesia and analgesia. The treatment catheter is removed and replaced by a standard urethral drainage catheter, which remains for 4–17 days.[39]

Transurethral laser coagulation of the prostate

Laser-induced coagulative necrosis of the prostatic tissue can be achieved either by surface application to the prostatic urethra in a technique

termed visual laser ablation of the prostate (VLAP) or by inserting specially designed fibres into the prostatic tissue via the urethra, termed interstitial laser coagulation (ILC). VLAP uses a neodynium:yttrium-aluminium-garnet (Nd:YAG) laser to create areas of coagulative necrosis extending out from the prostatic urethra. This laser has a unique wavelength of 1064 nm and penetrates tissue for up to 1.7 cm leading to delayed necrosis and sloughing of tissue into the urethra over a period of 6–8 weeks. For ILC, a diode laser is transmitted through a fine fibre, which is inserted into the prostate under endoscopic control to a depth of 1 cm to create 3 cm^3 lesions within 2–3 minutes at a temperature of 85°C. Typically, up to ten locations can be treated, with the procedure lasting for 30–60 minutes under local anaesthesia. Catheterisation is typically required for between 3 and 7 days.[40]

Identification of patient subgroups and criteria for treatment

The one-off outpatient nature of minimally invasive therapy makes it an attractive option for men with moderate to severe LUTS who do not wish to have long-term medical treatment or who are concerned about the side effects of more invasive treatments. The reduced need for anaesthesia and lower morbidity make it suitable for men with extensive co-morbidity.[27] These procedures are generally not suitable for men with larger prostates (> 50 g) because of prolonged treatment time and high rates of post-treatment dysuria and urinary retention. In addition, they are not indicated for men with absolute indications for prostate surgery such as urinary retention, bleeding and recurrent urinary infection. The use of stents is restricted to men with urinary retention with extensive co-morbidity, which precludes prostate ablation techniques.

Personnel involved

Most of these treatments can be performed by a single physician, typically a urologist, in an office or clinic setting. The physician should have expertise in both the technique and the administration of local anaesthetic. A nurse assistant is also required together with appropriate reception and administration staff. Removal of the catheter can be performed at a subsequent office visit or by a community nurse.

Setting

These technologies are suitable for use in the office, clinic or ambulatory care facility with a typical stay of approximately 4–8 hours. For procedures performed under local anaesthetic a well-equipped clinic room with basic resuscitation facilities, appropriate utility supply and recovery area are all that are required; however, for some procedures a standard operating theatre set-up with anaesthetic support is required. High capital costs and concerns regarding effectiveness have led to low use of these procedures in the UK, with only a few centres using the technology. It is estimated that fewer than 1000 procedures in total are carried out per year, representing less than 4% of the total.

Equipment

In general, these technologies require a generator and a delivery device, which is typically a single-use modified urethral catheter. In addition, some require cooling circuits, endoscopic positioning and transrectal imaging for device placement and monitoring of effect. Drugs and delivery equipment for local anaesthesia and sedation are also required. Patients are generally discharged home shortly after completion of the procedure with an indwelling catheter. Different manufacturers offer competing devices, which differ mainly in power output and delivery system. For TUMT the main devices are Prolieve™ (Boston Scientific, USA), CoreTherm™ (Prostalund, Sweden), TherMatrx® (American Medical System, USA), and Prostatron® and Targis™ (Urologix, USA). TUNA is provided by Prostiva™ (Medtronic, USA), WIT by AquaTherm™ (WIT) (ACMI, USA) and HIFU by Sonablate® 500 (Focus Surgery, USA). The currently available interstitial laser device is Indigo Optimax (Indigo LaserOptic™(Johnson & Johnson, USA).[40,41] The available prostatic stent is marketed as Urolume® (American Medical System, USA).

Costs

The cost of a TUMT generator is approximately £14,000, with an additional cost of disposables of approximately £350 per case (Urologix, USA). The TUNA machine costs £5750 with an additional cost of £700 for the disposable cartridge (Medtronic, UK). The purchase cost of the Sonablate 500 HIFU system is around £300,000 (UK HIFU). Urolume stents cost £1365 (American Medical System, UK). The remaining devices are not marketed in the UK.

Transurethral resection of the prostate (TURP)

Introduction

TURP has been the standard method of surgical management of clinical BPE for 50 years and in recent times has accounted for more than 90% of

prostatectomies performed for this indication,[42] although in current practice this has been reduced to 60–80% by the advent of other ablative procedures detailed below.[42] The technology uses diathermy current for prostate resection via a loop electrode using a continuous flow endoscope passed down the urethra with non-ionic fluid irrigant, usually 1.5% glycine. Coagulative haemostasis is achieved during and at the end of the procedure with a ball diathermy electrode. For most men a skilled urologist can achieve complete resection of up to 100 g of tissue within 1 hour. Improvements in endoscope design, diathermy units and bladder irrigation have reduced both operating time and risk of major morbidity. Postoperatively the bladder is irrigated for 6–24 hours; the catheter is removed at 24–48 hours after surgery before discharge home.[43]

Identification of patient subgroups

TURP is a versatile technique that can achieve effective relief for men with bothersome moderate or severe symptoms. It is also highly effective at treating other manifestations of BPE such as urinary retention, recurrent infection and haematuria. Blood loss and absorption of irrigant fluids are the main causes of operative morbidity, particularly in men with clotting disorders, those taking anticoagulant or antiplatelet medication and those with significant cardiovascular morbidity. Safety can be improved by use of preoperative drug treatment aimed at reducing both the size of the prostate and bleeding during the procedure and use of preoperative antibiotic prophylaxis. Improvements in spinal anaesthesia and better videoendoscopic equipment have resulted in shorter operation times, and more aggressive catheter removal policies have shortened hospital stay.[44]

Personnel involved

TURP requires full operating room facilities with a urologist, scrub and circulating nurses and an anaesthetist. Standard inpatient pathways with experienced ward and recovery room staff and porters are also required.

Setting

Traditionally TURP was considered an inpatient procedure requiring admission the day before surgery and a 4-day postoperative stay in a urology hospital ward. In the UK, the last 1–2 years have seen the development of managed care pathways and a drive towards shortened hospital stay, stimulated partly by competing techniques and partly by cost containment and avoidance of hospital-related morbidity. This has meant that stay for straightforward TURP has been shortened to 2–3 days with discharge the morning following midnight catheter removal.[44]

Equipment

A standard diathermy generator is required with cutting and coagulation outputs. The videoendoscopic equipment is also standardised with, typically, a 26Fr sheath, operating element, 30° telescope, xenon light source and 'two-chip' camera with appropriate monitor.

Costs

Multiple manufacturers compete for this market, which tends to keep actual purchase costs low although list prices are high. Most of the equipment would be considered standard operating department stock with multifunctionality for use in open surgery, endourology and laparoscopic surgery. Within the NHS the procedure has unique Healthcare Resource Group codes, L27 for men aged over 69 years and L28 for men aged under 70 years, with mean costs (2004–2005) set by providers of £2060 (interquartile range £1715–2429) and £1864 (interquartile range £1547–2198) respectively.[45]

Transurethral incision of the prostate

Endoscopic incision of the prostate from bladder neck to verumontanum at the 7 o'clock position using cutting diathermy via a standard resectoscope is a relatively simple technique that is claimed to have short-term equivalence in effectiveness to TURP for men with smaller prostates (< 30 g).[46,47] The advantages of transurethral incision of the prostate (TUIP) are reduced bleeding with no need for postoperative irrigation and shortened catheterisation time together with a lower risk of developing retrograde ejaculation.[47] The disadvantage is that no prostatic tissue is removed leading to a high rate of symptom recurrence and need for further surgery.[43]

Patient selection, personnel required, setting, equipment and costs are similar to those for TURP.[24,45] TUIP has a specific OPCS-4 code (M66.2) and data from the NHS suggest that 2464 procedures were carried out in England during 2005, representing 8.5% of the total (main operation four-character codes 2004–2005).[22]

Other tissue ablative techniques

Vaporisation of the prostate

Introduction

Vaporisation of tissue requires rapid localised heating to temperatures of 100°C or more with minimal depth of penetration. The anatomy of the prostate and in particular the development of hyperplasia within the inner periurethral zones of the gland mean that transurethral delivery of energy for vaporisation is both feasible and desirable. At present two alternative sources of energy are available for transurethral vaporisation of the prostate (TUVP): laser and electrosurgical.[48]

Interventions using laser technology

Transurethral laser vaporisation of the prostate

Basic research has enabled the identification of lasers with source, wavelength and absorption characteristics suitable for rapid heating with minimal tissue penetration that could be delivered by the transurethral route and cause vaporisation on contact with the prostate.[49] Initially, Nd:YAG was used at a power setting of 40 W.[50] This had a disadvantage for vaporisation purposes of relatively deep tissue penetration (4–18 mm) related to low absorption and a wavelength of 1064 nm in the invisible spectrum.[51] These characteristics were improved by passing the Nd:YAG-generated beam through a potassium-titanyl-phosphate (KTP) crystal, which doubles the frequency and halves the wavelength. By doing so, the light becomes visible in the green spectrum (532 nm), which encourages absorption by haemoglobin[52] and results in a depth of penetration ranging from 0.8 to 3 mm.[49] In a highly vascular tissue such as BPE, this results in a high energy density and rapid vaporisation, which is further improved by the higher power source (80 W) that is currently available for this technology.[51] The holmium laser can also be used for transurethral prostate vaporisation by delivering energy at a wavelength of 2140 nm.[53] This laser has limited tissue penetration (0.4 mm), affords excellent haemostasis and is preferentially absorbed by water, enhancing the effectiveness of tissue ablation. Initially, moderate power (60 W) was used but this has now been increased to 80–100 W to improve efficiency.[49] Contact laser vaporisation is performed using an irrigating cystoscope but still requires similar anaesthesia and operating conditions to TURP, with the operating time increased by a factor of approximately 1.5.[54]

Interventions using non-laser technology

Transurethral electrovaporisation of the prostate

This technique utilises a standard monopolar electrodiathermy device to deliver sufficient power, typically 180–300 W on the 'cut' setting, to vaporise tissue on contact. The procedure is performed using an irrigating sheath and telescope passed along the urethra, which allows continuous flow of a non-ionic solution such as 1.5% glycine to maintain a clear view. The current is delivered through a grooved ball or modified loop electrode giving a depth of penetration of 1–3 mm.[55,56] The procedure is similar to TURP in terms of requirement for spinal or general anaesthesia, operating time and aftercare.[55,57] More recently, further modification has allowed the use of bipolar current, which enables the use of physiological saline as a safer irrigant with tissue effects occurring at lower temperatures (ranging from 40°C to 70°C) than with monopolar electrosurgery (300–400°C).[58,59]

Identification of patient subgroups and criteria for treatment

The requirement for general anaesthesia and standard operating room conditions and the degree of invasiveness mean that indications for vaporisation surgery in terms of symptom severity, symptom bother and degree of co-morbidity are similar to those for TURP. The simultaneous haemostatic coagulating effect of vaporisation techniques suggests additional usefulness for men on long-term anticoagulant or antiplatelet therapy who may have been previously advised against TURP.[60] The increased operating time compared with resection procedures, however, suggests that these techniques are most suited to small or medium-sized prostates up to approximately 60 ml. The lack of tissue samples means that prostate cancer should be excluded when necessary by preoperative investigation.

Personnel involved

Vaporisation of the prostate requires standard operating room preparation and facilities. Patients will be admitted to a hospital bed or ambulatory care facility and prepared for surgery by nursing and ancillary staff with preceding anaesthetic assessment. On transfer to the operating room, the anaesthetist and assistant will administer the appropriate anaesthetic. The urologist, supported

by a scrub nurse and two circulating nurses, carries out the surgery. Following completion, the patient is transferred to a staffed recovery room and then back to the ward setting to complete the hospital stay, which is typically 2 days. If discharged with an indwelling catheter this will require planned removal by a hospital or community-based nurse.

Setting
In the UK the procedure will be carried out through an inpatient urology unit, typically with day of surgery admission and subsequent single overnight stay. Some units have set up US-style ambulatory care facilities to restrict the hospital stay to less than 24 hours if clinically and socially appropriate. It is difficult to give precise figures concerning the number of such procedures performed under the NHS because of imprecise coding but it is likely to be fewer than 5000, representing less than 17% of the total.

Equipment
For electrovaporisation, the only equipment that is required in addition to that used for TURP is the modified ball or loop electrode, which is currently designed for single patient use. For laser vaporisation, a source generator is required together with laser fibres, which are generally single patient use, and protective eyewear.

Costs
In comparison with TURP, electrovaporisation requires a more expensive modified electrode (Gyrus, UK), typically three times the cost of the standard loop and ball electrode (£40) used for TURP. The major cost for laser vaporisation is the capital purchase of the source generator, which ranges from £90,000 for the KTP laser (Laserscope, Cwmbran, UK) to £120,000 for the holmium laser (Sigmacon, Stanmore, UK), together with single-use fibre costs of £750 and £550 per patient respectively. The main cost saving (and associated gain in benefits) is reduced requirement for blood transfusion. With modern care pathways, hospital stay is likely to be 1 day less than for TURP.

Resection of the prostate
Introduction
These techniques seek to create a similar tissue ablative effect to TURP but with reduced bleeding and fluid absorption leading to lower perioperative morbidity. Modified irrigating cystoscopes or resectoscopes are used and the prostate is removed piecemeal as in TURP allowing subsequent histological examination. At present this can potentially be achieved either by holmium:YAG laser resection or by bipolar electroresection using normal saline.

Interventions using laser technology
Holmium:YAG laser prostatectomy
Holmium laser prostatectomy used to be performed by resection of small pieces of prostate tissue down to the prostate capsule (HoLRP); however, this technique has largely been superseded by holmium laser enucleation of the prostate lobes (HoLEP). HoLEP uses the laser to dissect in the surgical planes and is conceptually the endoscopic equivalent of open prostatectomy. In this technique the holmium laser is used at a high power setting of 60–80 W with an end-firing fibre[61]. The procedure is performed using a continuous flow resectoscope with a video system and saline irrigation to maintain a clear view. The laser fibre is passed through a stabilising catheter with 5–10 cm of cladding stripped off at the distal end. Typically, the laser is set at an energy of 2 J and a frequency of 50 Hz, with minor variations depending on the preference of the surgeon. The procedure starts with bladder neck incisions at 5 and 7 o'clock to define surgical margins. The median and lateral lobes are then undermined and resected off the prostatic capsule in a retrograde direction until the bladder neck is reached. The resected lobes are pushed into the bladder, morcellated and removed. The procedure can be carried out under spinal or general anaesthesia, with slightly longer operating times than for TURP but with similar postoperative care.[51,62–64]

Interventions using non-laser technology
Bipolar resection of the prostate
The technique of bipolar electroresection requires a diathermy generator (200 W capability, a radio frequency range of 320–450 kHz and a voltage range of 254–350 V) and a cutting loop that is similar to a monopolar loop in shape but which has the active and return electrode on the same axis separated by a ceramic insulator. A chip in the loop automatically adjusts the power setting of the generator for the best cutting and coagulating parameters.[65] The underlying principle of this technique is the conversion of conductive solution into vapour (plasma) containing energy-charged particles that cause molecular dissociation of tissues. The electric arc (charged particles) takes the path of least resistance, the saline irrigant, thus controlling temperatures at the treatment site and reducing the risk of thermal damage to the surrounding tissue.[58,66] The procedure is performed using a continuous flow resectoscope with saline

irrigation reducing the risks of fluid absorption and blood loss.[67]

Transurethral vaporesection of the prostate
Transurethral vaporesection of the prostate (TUVRP) involves simultaneous resection and vaporisation with coagulation of prostatic tissue. The main differences between standard TURP and TUVRP are in the design of the loop and the level of electroenergy used. In TUVRP, a thick band-like loop is coupled with a high electrosurgery cutting energy. The perceived advantages of TUVRP are shorter duration of catheterisation and hospital stay, less blood loss, better visualisation during resection and reduced electrolyte disturbances.[68] The main disadvantage of TUVRP is longer duration of the procedure because of slower passage of the band electrode to allow for maximum coagulation and desiccation of the prostatic tissue, which remain central to this technique.

Identification of patient subgroups and criteria for treatment
The selection of patients, preoperative workup, informed consent, type of anaesthesia, postoperative care and clinical follow-up are similar to those of TURP. If appropriate, prostate cancer should be excluded by biopsy before proceeding with HoLEP.[69] Improved haemostasis with these techniques encourages their use for men with clotting abnormalities or those taking anticoagulant or antiplatelet drugs. There is some suggestion that this procedure is suitable for prostate enlargement of any size.[51,64] A long learning curve and 20–30% longer operative time than for standard TURP mean that increased surgeon expertise and operating room availability are required.[70,71]

Personnel involved
Resection of the prostate requires standard operating room preparation and facilities. Protective eyewear is worn by surgeons, theatre personnel and patients to avoid eye damage from the laser. Before carrying out the procedures the laser machine is checked by trained theatre personnel according to the manufacturer's instructions. Patients will be admitted to a hospital bed or ambulatory care facility and prepared for theatre by nursing and ancillary staff with preceding anaesthetic assessment. On transfer to the operating room, the anaesthetist and assistant will administer the appropriate anaesthetic. The urologist carries out the surgery supported by a scrub nurse and two circulating nurses. It is difficult to define how many procedures a surgeon must perform to become competent but it is generally agreed that about 30 cases are required for a urologist familiar with transurethral surgery to feel reasonably safe performing the HoLEP technique. Following completion, the patient is transferred to the staffed recovery room and then back to the ward setting to complete the hospital stay, which is typically 2–3 days. If discharged with an indwelling catheter this will require planned removal by a hospital or community-based nurse.

Setting
In the UK, laser resection and transurethral resection (in normal saline) procedures will be carried out through an inpatient urology unit, typically with day of surgery admission and subsequent single overnight stay. Some units have set up US-style ambulatory care facilities to restrict hospital stay to less than 24 hours if clinically and socially appropriate. It is unclear how many of these procedures are performed in the UK but it is likely to be fewer than 2500 per year, representing less than 9% of the total.

Equipment
For laser resection of the prostate using holmium:YAG lasers, in addition to a high-power machine (100 W VersaPulse; Lumenis, USA), a 550-μm end-firing fibre, 6Fr ureteric catheter, morcellator and eyewear are required. The resection is performed using a 27Fr continuous flow resectoscope with a modified inner sheath for the laser fibre channel. The irrigating solution is 0.9% saline.[61,72] For bipolar resection in saline, a source generator and bipolar resection system with special cutting loops are required (Gyrus, USA).[65,67]

Costs
A HoLEP generator costs approximately £120,000, the tissue morcellator £20,000, laser fibre £550 and the morcellator blade £440.[51] However, a holmium:YAG laser can be efficiently used as a multifunctional endourological energy source in management of other conditions such as urinary stone disease, and the laser fibres and morcellator blades are designed for multipatient use. The main cost saving (and associated gain in benefits) is the reduced requirement for blood transfusion, possible shorter hospital stay and lower requirement for continuous postoperative irrigants.

Chapter 3
Description of care pathways

During the first half of the last century open prostatectomy was the only treatment option for BPE and because of significant mortality it was reserved for men with life-threatening problems such as urinary retention. The 1960s saw the advent of endoscopic transurethral techniques, particularly TURP, which allowed much safer surgery and widened treatment indications to include men with troublesome symptoms. Further improvements in perioperative care made TURP one of the most frequently performed operations towards the end of the twentieth century, particularly in the USA. Recent years have seen the increased use of drugs that can improve symptoms and possibly slow progression,[19,73] which has led to a decreased rate of surgical intervention, this being reserved for those who fail drug treatment or suffer complications.

The treatment strategy of reassurance followed by drugs followed by surgery is now standard in clinical practice and has been explored in previous reviews of cost-effectiveness.[74] A parallel development has been the trial of differing energy delivery technologies to achieve varying degrees of surgical prostate tissue ablation, with the aim of high efficacy and low morbidity to challenge the standard of TURP. In this field there have been many false dawns, with technologies being introduced in a haphazard and uncontrolled manner and then being abandoned, as the hoped-for advantages over TURP have not been realised. In the last few years, however, the application of randomised controlled trial (RCT) methodology to surgical treatments has stimulated a more evidence-based approach, partly driven by tighter regulatory requirements.

One deficiency of the current evidence, however, is the assumption that surgical treatment of BPE involves a single treatment over a patient's lifetime. This head-to-head comparative approach does not take into account the balance between short- or long-term effectiveness on one hand and morbidity and economic costs on the other, which differs between treatments, nor does it cater for the continued progression of the disease, which frequently results in the need for retreatment.

We therefore decided to formulate strategies consisting of sequences of escalating surgical intervention based on concepts underlying the ranking of particular treatments. A number of meetings were held between the clinical members of the research team to consider the likely place and use of each treatment modality in plausible strategies of management of BPE. These were then checked with colleagues within their respective urology units. Given funding constraints, formal consensus-building approaches such as the Delphi technique were not used. We first categorised treatments as being minimally invasive, typified by ambulatory care, reduced anaesthetic requirement and no tissue removal; tissue ablative, signifying the use of differing energy sources to remove prostate tissue; or standard, indicating TURP or TUIP. Again, using clinical consensus we defined plausible treatment sequences taking into account treatment mechanism and effect on the remaining prostate tissue. We similarly placed limits on the number of retreatments allowed based on current concepts of the use and effect of the differing procedures.

Figure 1 details plausible options of care informed by current clinical practice for a patient with BPE wanting surgery after a trial of drug therapy because the treatment has not resulted in symptomatic benefit or as a result of disease progression after initial benefit from drug treatment. The patient could be offered a minimally invasive intervention and if this results in symptomatic benefit no further treatment may be necessary. Should there be inadequate benefit or disease progression after initial benefit, the patient may be offered a choice of four other treatment options (drug therapy, repeat of minimally invasive intervention, a TURP or one of the other tissue ablative interventions such as KTP laser or TUVP). Should the patient have inadequate benefit or further disease progression after a second minimally invasive intervention, it was felt that the most plausible treatment option would be either a TURP or one of the other tissue ablative interventions. An alternative care pathway for a patient with BPE wanting surgery after a trial

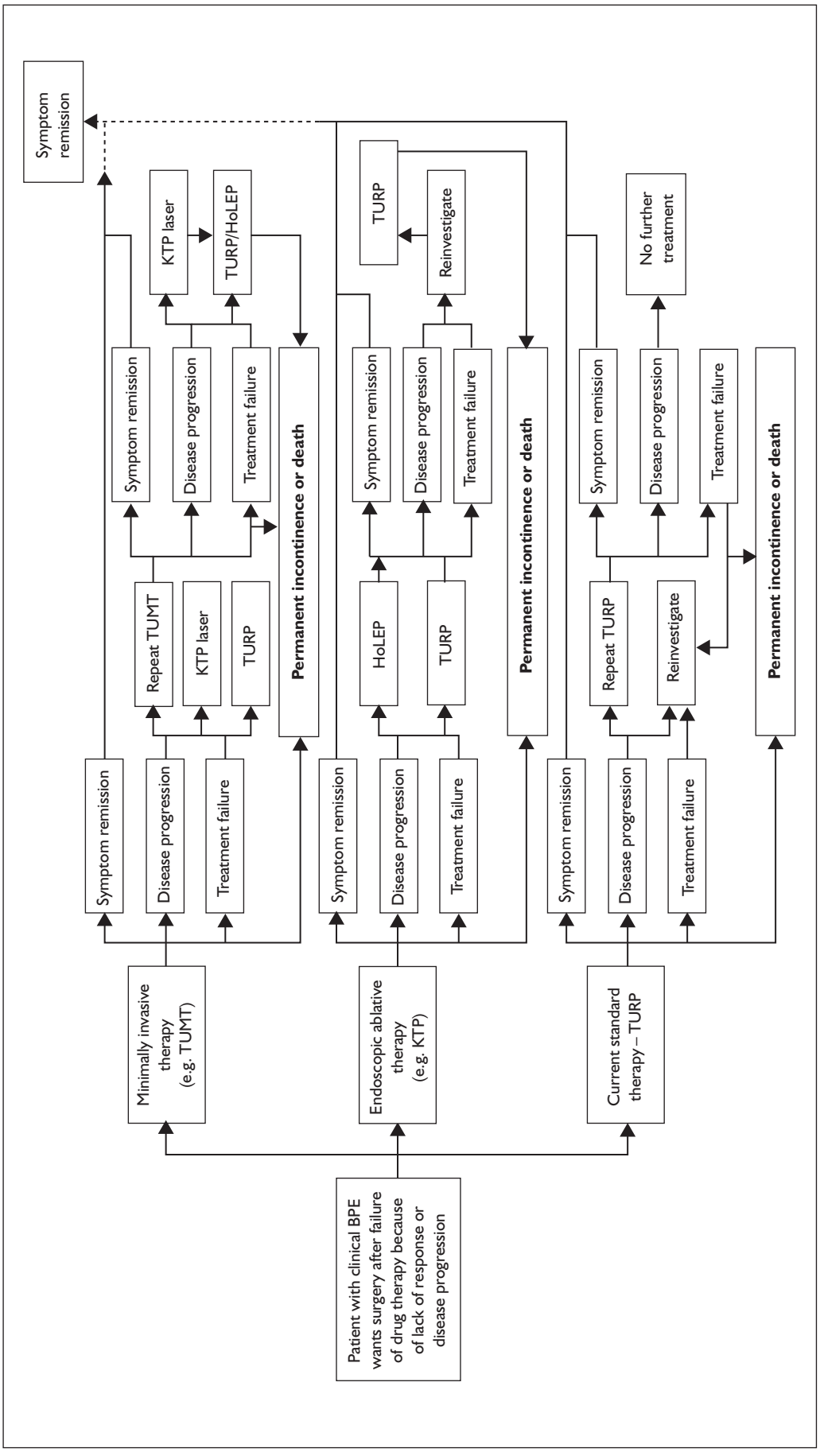


FIGURE 1 *Description of care pathways.*

of drug therapy would be to have one of the other tissue ablative interventions first, such as KTP laser or TUVP. Should there be inadequate benefit or disease progression after initial benefit, the patient may be offered a choice of another tissue ablative intervention or a TURP. Should the patient have inadequate benefit or further disease progression, one further TURP was allowed in the pathway.

One exception to this rule occurs when HoLEP, one of the other tissue ablative interventions, is the choice of treatment, because it is felt to be equivalent to open prostatectomy and, as such, no further ablative procedures are allowed for in the care pathway. If, on the other hand, a patient with BPE wanting surgery after a trial of drug therapy chooses to have the gold standard, TURP, then the only option allowed for in the care pathway should there be inadequate benefit or disease progression is a repeat TURP. Based on current clinical practice, a repeat TURP would usually be carried out only after reinvestigation, usually in the form of urodynamic assessment.

Chapter 4

Systematic review of previous economic evaluations

A technology is defined as being 'best' if it is the one that maximises the benefits (achieves the goals) that are intended by the decision-maker(s) from a given budget. Economic evaluation involves the comparison of cost and benefit for any technology change and thus provides a means of informing decisions about which technology is best.[75]

In this study the comparison between the different strategies depicted in the care pathways (see *Figure 1*) is made using a decision-analytic model (DAM).[75] The DAM is intended to show, first, the consequences in terms of costs and effects of each technology for the given population. These data are then used to inform the decision as to which technology or, when there is sufficient doubt, which technologies are the best, given current belief informed by evidence and judgement. Second, the DAM, in accounting for uncertainty, can be used to provide information about the likely value of conducting future research (evidence gathering) to reduce the uncertainty surrounding the decision about which technology or technologies are best.[75]

Sensitivity analysis might be used to show the effect on the results of the model of plausible variation in model structure or parameter values. Deterministic sensitivity analysis seeks to identify what change in a parameter value is required to produce a decision change. However, to account for parameter uncertainty with many parameters, each of which could have many values, it can be very difficult to interpret such thresholds. A solution is to use probabilistic sensitivity analysis.[76] Probabilistic sensitivity analysis can also be used to estimate the value of information (VOI), which can be used to inform decisions about further research (details of this method are available elsewhere[76,77]).

How such an economic evaluation of alternative surgical treatments for BPE might be conducted can be informed by a review of the existing literature. The purpose of the review was, first, to show the extent and results of current literature and, second, via a critique, to learn lessons in order to conduct the most appropriate economic evaluation to aid decision-making.

The following is a list of the information requirements for all DAMs:

- the population
- the technologies to compare
- the epidemiology: model structure (relationship between parameters)
- the epidemiology: parameterisation of the model (effectiveness, complications, utilities and costs)
- sensitivity analysis.

This list of requirements will form the framework used in this chapter to critique existing models and then in Chapter 11 the model used in this evaluation.

Because of deficiencies in any of the DAM information requirements, the results of existing economic evaluations were extremely unlikely to be sufficient to inform a decision now. Therefore, the only studies that were critiqued were those that considered at least some of the surgical treatments for men with moderate to severe symptoms of BPE and no complications, and which estimated outcomes using a DAM.

Search strategy

The following databases were searched for information on economic evaluations and quality of life: MEDLINE (1966–March Week 2 2006), EMBASE (1980–2006 Week 11), MEDLINE In–Process (20 March 2006), ISI Science Citation Index (1981–1 March 2006), Health Management Information Consortium Database (March 2006), NHS Economic Evaluation Database (March 2006) and HTA database (March 2006). In addition, recent conference proceedings of the European Association of Urology, American Urological Association and British Association of Urological Surgeons were searched. Reference lists

of all included studies were scanned to identify additional potentially relevant studies. Full details of the search strategies used are documented in Appendix 1.

The results of the literature searches, after deduplication against the Ovid multifile search, are presented in *Table 2*.

Studies selected for critique

Three studies published in six papers that contained data relevant to formulation of the DAM were identified. One study by Ackerman and colleagues was published in three papers,[78–80] and another by DiSantostefano and colleagues was published in two papers.[74,81] The third study by Howard and Wortley was published as a technology assessment report for the Australian Medical Services Advisory Committee (MSAC).[82]

Population

All three studies considered essentially similar populations, although DiSantostefano and colleagues and Ackerman and colleagues, in considering drug treatment and watchful waiting, actually considered a broader population. Ackerman and colleagues considered a cohort aged 65 years, Howard and Wortley did not state age, and DiSantostefano and colleagues considered the effect of varying age from 45 to 85 years.

Technologies

DiSantostefano and colleagues and Ackerman and colleagues compared TUMT and TURP in addition to drugs whereas Howard and Wortley compared TUMT with TURP. None compared strategies, i.e. what is the best sequence of treatments if, on failure or relapse (judged in some way), another procedure is planned. Instead they all assumed that should the initial treatment fail then there would be some chance of further treatment, which for all three studies was TURP. However, if the choice of initial treatment is at all dependent on the outcome of any future treatments then there is a need to consider the outcome of these future treatments in the economic evaluation. Of course, there might also be reason to consider repeating a procedure such as TUMT instead of using TURP immediately on failure or switching to a different procedure such as TUVP.

The epidemiology: model structure

To find the best technology, costs and consequences (including utility) must be estimated for each technology. Individual variability for a given population and technology implies that the various health-related events (e.g. degree of symptom improvement, death) that can occur over time must be expressed as probabilities. Therefore, the model estimates the expected ('average') cost and utility for the population. However, the complexity of patient pathways prevents specification of a

TABLE 2 *Results of the search for studies on cost-effectiveness*

Database	Hits screened	Selected for full assessment
MEDLINE/EMBASE/MEDLINE Extra multifile search (after deduplication in Ovid)	1213	65
ISI Science Citation Index	88	3
NHS Economic Evaluation Database	45	0
HTA database	21	12
Health Management Information Consortium Database	31	2
Selected from conference abstracts	6	0
Total	1404	82

probability distribution for every pathway. One solution is a Markov model,[83] in which events are reduced to a set of discrete health states of fixed duration (cycle length). An individual may only be in one health state at a time and at the end of each cycle they face the probability of making the transition to another health state. The individual will continue moving between health states until the prespecified number of cycles has been reached or until the individual moves into an absorbing health state (normally death) from where further transitions are not possible. This enables the calculation for each strategy of the expected value of cost and utility. These expected values are the sum of the value of the cost and utility for each state multiplied by the number of cycles spent in that state.

All three studies used a Markov model. The time horizon was 5 years for Ackerman and colleagues and 20 years for the other two studies. Cycle length was 3 months for Ackerman and colleagues, 6 months for Howard and Wortley and 1 year for DiSantostefano and colleagues, thus giving 20, 40 and 20 cycles respectively. The number of health states considered were 25, four and nine respectively.

The epidemiology: parameterisation of the model

No study claimed to have conducted a systematic review of the literature, although Ackerman and colleagues used the term 'comprehensive review'.

Effectiveness

One advantage of the simple 'chance' approach to second treatments is that the probability of failure can be simply assumed to be the probability of reoperation. However, the decision-making criteria underlying reported reoperation probabilities are usually unknown and different criteria might mean different outcomes. DiSantostefano and colleagues derived estimates of treatment failure ('no improvement') from the 1994 Agency for Health Care Policy and Research (AHCPR) guideline[19,84] and of reoperation for TURP from the AUA guideline[19,85] for the period up to 2000. Reoperation rates for TUMT were derived from two RCTs.[86,87] However, the AHCPR guideline is over 10 years old and its authors admit that very few studies reported symptom scores and that those that did used many different methods.[84] Although this limitation is allowed for to some extent in the wide confidence interval (CI) for this estimate (see Accounting for uncertainty in Chapter 10, p.112), the relationship between degree of symptom improvement and probability of retreatment is unclear. For example, do those who are counted as successful and who thus receive no further treatment continue with, 'on average', almost complete symptom relief or was the change only just sufficient to warrant no further treatment? For those who fail but receive no further treatment, it was not clear to what extent this was because the clinician believed that further treatment would not work or because further treatment was refused by the patient. It was also not clear why those who receive TURP have an annual probability of relapse ('disease progression') of about 1%, but those who receive TUMT cannot relapse.

Howard and Wortley used a single RCT[82] for TURP and several sources for TUNA to estimate 'early treatment failure' (within 6 months). Longer-term failure rates (equivalent to relapse) were stated to come from an RCT and a cohort study for TURP with a 10-year follow-up. For TUNA, data were derived from the percentage undergoing retreatment after 5 years.

Ackerman and colleagues used the same definition of treatment success for all treatments: 'significant improvement, achieving a 50% or greater decrease in the AUA symptom score; moderate improvement, achieving a 30–49% decrease in the AUA symptom score; minimal improvement, a less than 30% decrease in the AUA symptom score'. They cited various publications, as well as the 'multispeciality clinical panel', as sources for their probability of each degree of success, although it is not clear how these sources were synthesised. These probabilities were stated to be time dependent, although not all estimates were shown: the 5-year probabilities of 'success' for TURP and TUMT were 0.85 and 0.65 respectively.

Ackerman and colleagues[78] and DiSantostefano and colleagues[74,81] also had health states with different degrees of symptoms. However, this refinement would be important only if the choice of states that have differential effects on outcome is contingent on the symptom level. For example, if on day one 90% have some success such that they receive no further treatment for the next 10 years, it makes no difference whether half of them spend that time in a state of 'mild' symptoms and half in a state of 'no' symptoms or whether all of them spend that time in a single state, as long as the outcome of

that state is equal to the average of the outcome of 'mild' and 'no' symptoms, each weighted by 50%.

Complications

All models consider the possibility of complications, the most comprehensive being that of Ackerman and colleagues.[78] However, depending on the source of estimates, it is possible that there could be some unnecessary and perhaps misleading inclusions. For example, DiSantostefano and colleagues argue against the inclusion of differential mortality rates because either there is no difference between treatments or the difference is so small that to try to estimate would lead to bias.[74,81] This is backed up by long-term studies;[85] the same argument can be made for life-threatening complications such as myocardial infarction (MI).

Retrograde ejaculation occurs as a result of removal of prostate tissue by whatever means and does not significantly lower the utility value of successful treatment and is not associated with any costs. Erectile dysfunction (ED) following prostate surgery is a difficult and controversial issue: the meta-analysis presented later and previous systematic reviews have shown no statistically significant difference in occurrence between types of surgery. For the purposes of the cost-effectiveness analysis modelled over a 10-year period, we chose not to include ED as a complication as it was more likely to be caused by other concurrent, randomly distributed disease processes than the interventions under consideration. In addition, there is increasing evidence of an association between ED and urinary symptoms that would also confound estimated rates.

Utilities

All three studies used cost-utility analysis (CUA) and each had a utility of 1 for some states reflecting either 'significant improvement' or 'remission' and of 0 for death. Only Ackerman and colleagues[78] elicited preferences using the standard gamble approach[75] to estimate utilities for each of their other health states; however, their sample was small (only $n = 6$ or $n = 7$ for each of the 'risk averse' and 'non-risk averse' groups). Such data may be unreliable as they are based on so few observations. They may also not be comparable with utilities calculated for other patient populations – a larger sample from the general public would have been better. DiSantostefano and colleagues[74,81] used utilities from a variety of sources, including Ackerman and colleagues[78] for incontinence. Howard and Wortley simply used opinion (they do not state the source) and values for treatment success (as full health, i.e. 1) for failure (0.9) or side effects (0.95).[82]

Costs

All three studies estimated costs in at least the categories of 'procedure', 'complications' and 'failure' (implying the inclusion of reoperation costs). However, Howard and Wortley and Ackerman and colleagues simply used estimates for each category and provided no further breakdown. DiSantostefano and colleagues provided a slightly fuller breakdown by resource use for each procedure such as number of physician visits. However, none of the studies differentiated between procedure and hospital stay and none expressed cost of equipment as a function of its lifetime or reusability.

Sensitivity analysis

All three studies performed some deterministic sensitivity analyses. Only DiSantostefano and colleagues used probabilistic analysis for parameter uncertainty.[74,81] Their distributions for probability of treatment failure, reoperation and complications were estimated appropriately using beta distributions. They stated that they were parameterised using the 95% confidence intervals from various sources, for example the AUA meta-analysis,[85] and presumably used the means from these sources. The distributions for their cost estimates were assumed to be normal and parameterised from US national databases for TURP and TUMT: they stated that the standard deviation was used, but the appropriate statistic is the standard error. Given the likely large sample size of these databases, the standard deviation would probably considerably overestimate the uncertainty, although this is a matter of judgement.

Conclusion

Previous studies have attempted to address the challenges of constructing a DAM for BPE surgical treatments. All of these studies had some limitations, which have been discussed. Taking these limitations into account it is suggested that a future DAM should:

1. include more single treatments and treatment strategies
2. develop methods to estimate the probability of failure using clinical criteria relevant to the UK, comparing the effect of this with simply using reoperation rates
3. develop methods to estimate utilities that more explicitly use the main outcome of effectiveness evidence, the IPSS
4. include relevant complications and mortality rates for the UK
5. provide a breakdown of costs that is sufficient to estimate the independent effects of procedure cost, hospital inpatient stay and purchase of any new equipment
6. conduct sensitivity analysis deterministically when appropriate and with probability distributions for all relevant parameters, obtained by explicit methods in accordance with theory and best practice.

When developing the economic model published in Chapter 10, consideration was given to how these limitations could best be avoided or minimised.

Chapter 5

Methods of, and studies included in, the systematic reviews of clinical effectiveness

Methods for reviewing effectiveness

Search strategy

Electronic searches were undertaken to identify published and unpublished reports of RCTs evaluating the effectiveness of established and new interventional treatments for the management of symptoms and complications subsequent to BPE. Searches were not restricted by publication year or language and included conference proceedings.

The databases searched were MEDLINE (1966–September Week 3 2006), EMBASE (1980–2006 Week 38), MEDLINE In–Process (27 September 2006), BIOSIS (1985–22 September 2006), ISI Science Citation Index (1981–23 September 2006), ISI Proceedings (1990–18 March 2006), Cochrane Controlled Trials Register (CENTRAL) (The Cochrane Library, Issue 1, 2006), Cochrane Database of Systematic Reviews (The Cochrane Library, Issue 1, 2006), Database of Abstracts of Reviews of Effectiveness (March 2006), HTA database (March 2006), National Research Register (Issue 1, 2006), Clinical Trials (March 2006) and Current Controlled Trials (March 2006). In addition, recent conference proceedings of the European Association of Urology, the American Urological Association and the British Association of Urological Surgeons were searched. Reference lists of all included studies were scanned to identify additional potentially relevant studies. Full details of the search strategies used are documented in Appendix 1.

All titles and abstracts identified in these ways were assessed to identify potentially eligible studies. Two reviewers independently assessed them for inclusion, using a study eligibility form developed for this purpose (see Appendix 2). Any disagreements were resolved by consensus or arbitration.

Inclusion and exclusion criteria

Types of studies

Individual RCTs were eligible for inclusion irrespective of publication language if they assessed interventional treatment options for the treatment of BPE. Initially, it was intended to include population-based observational studies with a minimum follow-up of 3 years but this was subsequently deemed not to be necessary as long-term follow-up data from RCTs was sufficient to provide more robust estimates of rare complications and effectiveness. Abstracts were considered only when no full-text RCTs were available for a particular intervention.

Types of participants

Trials of men with a clinical diagnosis of BPE who have undergone surgery were included. Patients undergoing conservative management (watchful waiting or medical therapy) were excluded.

Types of interventions

Methods of surgical intervention for BPE included:

- minimally invasive techniques
  - transurethral microwave thermotherapy (TUMT)
  - transurethral needle ablation (TUNA) of the prostate
  - stents
  - high-intensity focused ultrasound (HIFU)
  - transurethral ethanol ablation of the prostate (TEAP)
  - water thermotherapy (WIT)
  - transurethral laser coagulation of the prostate
- transurethral incision of the prostate (TUIP)
- transurethral resection of the prostate (TURP) – reference standard
- other tissue ablative techniques
  - transurethral laser prostatectomy – resection

  - transurethral laser prostatectomy – vaporisation
  - bipolar TURP
  - transurethral electrovaporisation of the prostate (TUVP)
  - bipolar TUVP
  - transurethral vaporesection of the prostate (TUVRP)
  - bipolar TUVRP.

Types of outcomes

Data were sought to describe both short-term and long-term outcomes. The following measures of outcomes were sought for different follow-up periods (3, 6 and 12 months or longer):

Primary outcome

- symptom score.

Other outcomes

- urodynamic
  - peak urine flow rate
  - mean urine flow rate
  - total voided volume
  - residual volume
  - detrusor pressure
- complications
  - intraoperative complications
  - co-interventions
  - clot retention
  - cardiovascular events
  - transurethral resection (TUR) syndrome
  - blood transfusion
  - septicaemia
  - urinary retention
  - recatheterisation
  - urinary tract infection (including epididymitis)
  - irritative urinary symptoms
  - incontinence
  - retrograde ejaculation
  - erectile dysfunction
  - stricture
  - reoperation rate
  - mortality
- other
  - prostate size
  - quality of life score.

Data extraction strategy

The titles and abstracts of all papers identified by the search strategy were screened. Full-text copies of all potentially relevant studies were obtained and two reviewers independently assessed them for inclusion. Reviewers were not blinded to the study authors, institutions or sources of the reports. Any disagreements were resolved by consensus or arbitration.

A data extraction form was developed to record details of trial methods, interventions, participants' characteristics and outcomes (see Appendix 3). Two reviewers independently extracted data from the included studies. Any differences that could not be resolved through discussion were referred to an arbiter.

Quality assessment strategy

Two reviewers working independently assessed the methodological quality of the included full-text studies. Again, any disagreements were resolved by consensus or arbitration. Primary RCTs were assessed using an assessment tool, drawing on the schema suggested by the NHS Centre for Reviews and Dissemination,[88] Verhagen and colleagues,[89] Downs and Black[90] and the Generic Appraisal Tool for Epidemiology (see Appendix 4).

Data synthesis

For trials with multiple publications, only the most up-to-date data for each outcome were included. Dichotomous outcome data were combined using the Mantel–Haenszel relative risk (RR) method and continuous outcomes were combined using the inverse variance weighted mean difference (WMD) method. The results are all reported using a fixed-effects model. Chi-squared tests and *I*-squared statistics were used to explore statistical heterogeneity across studies and, when present, random-effects methods were applied. Other possible reasons for heterogeneity were explored using sensitivity analyses. The meta-analyses were conducted using the standard Cochrane software RevMan 4.2. Because of the lack of uniformity of the data presented by many studies, a qualitative review looking for consistency between studies was also performed.

Symptoms assessed with the IPSS and the AUA symptom index were considered equivalent and therefore trials reporting symptoms in these ways were combined. Studies reporting symptoms as Madsen–Iversen symptom indexes were analysed separately. The IPSS/AUA scale ranges from 0 to 35. Scores ranging from 0 to 7 are equivalent to mild symptoms, from 8 to 19 are equivalent to moderate symptoms, and from 20 to 35 are equivalent to severe symptoms.

A large prostate was defined as having an estimated weight of more than 40 g, a moderate-sized prostate a weight of between 30 and 40 g and a small prostate a weight of less than 30 g (Professor James N'Dow, University of Aberdeen, 2006).

As some complications could not be confidently separated into those reported in the immediate postoperative period and those experienced over the course of the trial, all reports of the same complication were pooled together regardless of the timing of occurrence. Also, for the purposes of this review, 'strictures' included bladder neck stenosis and urethral stricture as it was difficult to distinguish between them given the information provided in the trials and because definitions of these complications were inconsistent from report to report. Only blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in the results section as these were felt to be the most important for the economic model. Other outcomes are presented in the appendices.

In terms of urodynamic outcomes, only the results for peak urine flow rate are presented in the body of this report because clinical experts consider this to be a more precise measure of a urodynamic outcome. Other urodynamic outcomes were also analysed and are presented in the appendices.

Quantity and quality of research available

Number of studies identified

The search strategies identified 3794 study reports after removing duplicates (*Figure 2*). Of these, 621 (466 full text, 155 abstracts) were selected for further assessment (*Table 3*).

Number and types of studies included

In total, 158 reports met the inclusion criteria for the review and these described 88 RCTs (*Figure 2*). Apart from one,[91] which was an abstract, the primary reports of the studies were full-text papers.

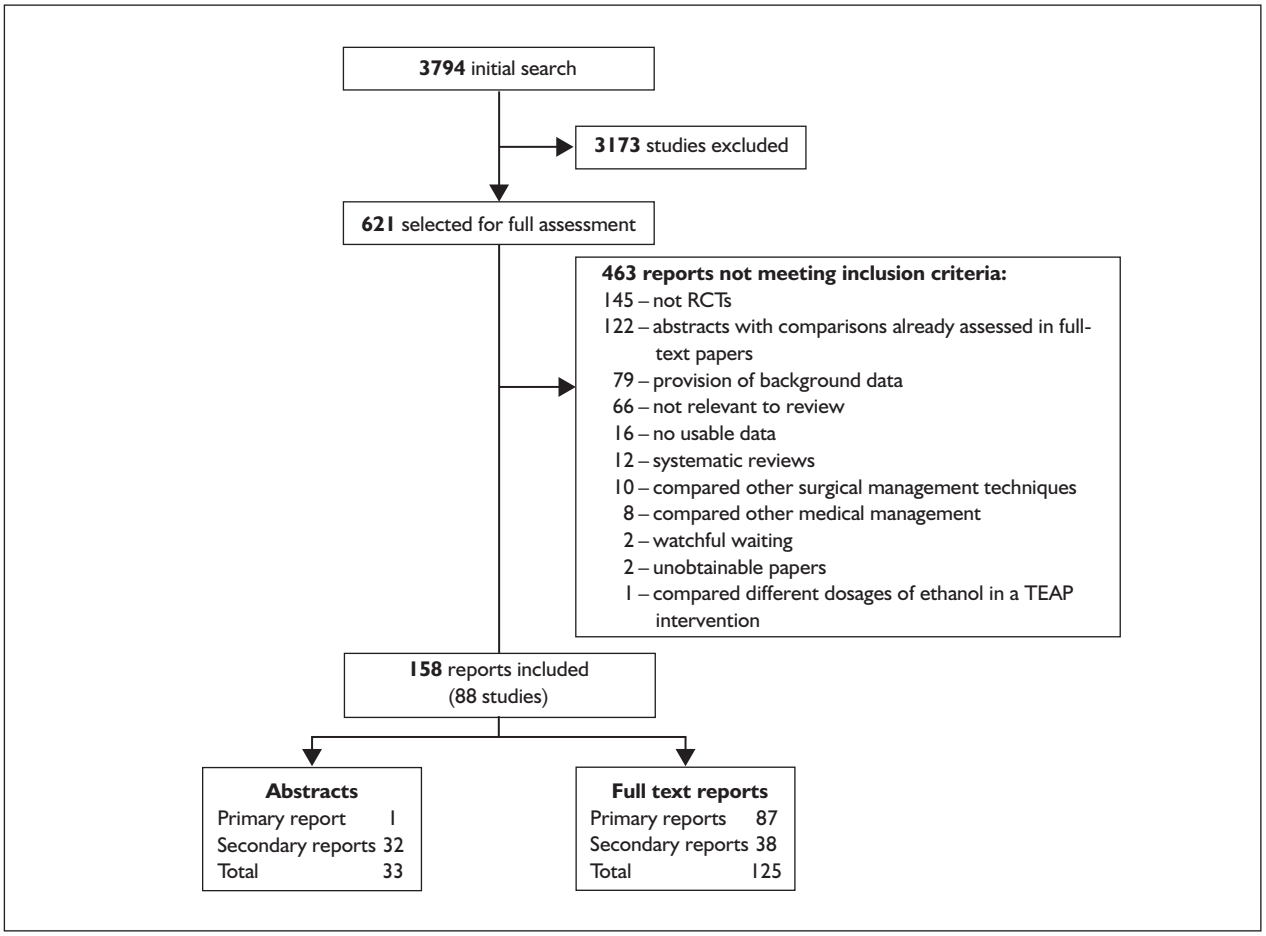


FIGURE 2 *Study selection process.*

TABLE 3 *Search results*

Database searched	Number selected
MEDLINE/EMBASE/MEDLINE In-Process multifile search (after deduplication in Ovid)	370
ISI Science Citation Index	52
BIOSIS	118
CENTRAL	8
Cochrane Database of Systematic Reviews	0
Database of Abstracts of Reviews of Effectiveness	4
HTA database	7
National Research Register	10
Current Controlled Trials	7
Clinical trials	0
Conference abstracts	45
Total selected	621

The included studies and associated references are listed in Appendix 5.

Number and types of studies excluded, with reasons for specific exclusions

In total, 178 reports were obtained but subsequently excluded because they failed to meet one or more of the inclusion criteria (*see Figure 2*). Of these, 145 were not RCTs. Of the 33 remaining reports, ten included comparisons involving other surgical management,[90,92–100] four included comparisons involving medical management for BPE,[101–104] two compared TURP with watchful waiting,[6,105] and one compared different dosages of ethanol within an RCT of transurethral ethanol ablation of the prostate.[106] An additional 16 reports had no usable data.[107–122]

Study quality

A summary of the quality assessment of the 88 full-text RCTs is presented in *Table 4* and the detailed quality assessment score for each of the included studies is reported in Appendix 6. The method of randomisation was unclear in the majority of the studies (75%); however, in one (1%),[123] an inadequate approach to sequence generation (alternation) was used. Suboptimal approaches to concealment of treatment allocation (serially numbered sealed envelopes) were used in 12 studies (14%).[57,124–134] It was unclear whether the groups were similar at baseline in seven studies (8%) with respect to the most important prognostic factors.[135–141] The eligibility criteria were clearly specified in all but one study.[142] In the majority of the studies (62%) the groups were treated in the same way apart from the intervention received, but this was unclear in 13 studies (15%).[136,138,139,143–151,167] In most studies (95%) follow-up was long enough to detect important effects on short-term outcomes (at least 3 months); however, only 69% of the studies followed up their participants for at least 1 year.

In the majority of the studies it was unclear whether outcome assessors, care providers and patients were blinded. Point estimates and measures of variability were presented in 88% of the studies, although in three studies it was unclear whether means or medians were used as the point estimate measure.[134,152,153] The dropout rate was unlikely to cause bias in 12 studies[124,138,150,154–162] but this information was unclear in 74 (85%) of the studies. Only 16 studies (18%) stated that an intention to treat analysis was performed; however, this seems questionable in 11 of these studies[57,70,125,130,136,139,145,154,163–165] as they failed to include the total number of participants in each arm in the subsequent follow-up assessments and an additional study stated that patients failing to complete the treatment or failing to return for follow-up were substituted.[124] It was unclear whether 67 other studies (77%) included an intention to treat analysis. It was also unclear in some studies how many patients were assessed at each follow-up. In 11 studies (13%) it was stated that the interventions were undertaken by someone

TABLE 4 *Summary of the quality assessment of the included randomised controlled trials* (n = *88)*

Criteria	Yes	No	Unclear
1. Was the assignment to the treatment groups really random?	21 (24%)	1 (1%)	65 (75%)
2. Was the treatment allocation concealed?	10 (11%)	12 (14%)	65 (75%)
3. Were the groups similar at baseline in terms of prognostic factors?	65 (75%)	15 (17%)	7 (8%)
4. Were the eligibility criteria specified?	84 (97%)	1 (1%)	2 (2%)
5. Was the intervention (and comparison) clearly defined?	81 (93%)	2 (2%)	4 (5%)
6. Were the groups treated in the same way apart from the intervention received?	54 (62%)	20 (23%)	13 (15%)
7. Was follow-up long enough to detect important effects on outcomes of interest?			
(a) For short-term outcomes, at least 3 months	83 (95%)	3 (3%)	1 (1%)
(b) For long-term outcomes, at least 1 year	60 (69%)	25 (29%)	2 (2%)
8. Were the outcome assessors blinded to the treatment allocation?	13 (15%)	5 (6%)	69 (79%)
9. Were the care providers blinded?	3 (3%)	7 (8%)	77 (88%)
10. Were the patients blinded?	15 (17%)	8 (9%)	64 (74%)
11. Were the point estimates and measures of variability presented for the primary outcome measures?	77 (88%)	7 (8%)	3 (3%)
12. Was the withdrawal/dropout rate likely to cause bias?	1 (1%)	12 (14%)	74 (85%)
13. Did the analyses include an intention to treat analysis?	16 (18%)	4 (5%)	67 (77%)
14. Was the operation undertaken by someone experienced in performing the procedure?	11 (13%)	6 (7%)	70 (80%)

experienced in performing the procedure; however, another 70 studies (80%) failed to provide this information for both types of intervention being delivered to the participants.

Characteristics of included studies

Appendix 7 provides details of the characteristics of the included studies. There were 94 relevant comparisons in the 88 eligible RCTs (8494 randomised participants); one trial had four arms and four trials had three arms (*Table 5*). In the following chapters an overview of the characteristics of the included studies for each identified comparison is presented.

Assessment of effectiveness

The assessment of effectiveness is reported in the following chapters, beginning with the minimally invasive techniques. No studies involved a comparison with HIFU and water thermotherapy. Three direct comparisons reported in three RCTs[204–206] between a minimally invasive intervention and other ablative interventions were identified. These are presented in Appendix 10.

TABLE 5 *Number of trials and participants for each intervention assessed*

Comparison	Number of trials	Participants	References
TUMT vs TURP	6	549	Ahmed *et al*., 1997;[124] Wagrell *et al*., 2002;[165] d'Ancona *et al*., 1998;[166] Dahlstrand *et al*., 1993;[167] Dahlstrand *et al*., 1995;[168] de la Rosette *et al*., 2003[169]
TUMT vs sham	11	1159	Bdesha *et al*., 1994;[125] Blute *et al*., 1996;[126] Ogden *et al*., 1993;[133] Abbou *et al*., 1995;[143] Larson *et al*., 1998;[159] Nawrocki *et al*., 1997;[160] Albala *et al*., 2002;[170] Brehmer *et al*., 1999;[171] de Wildt *et al*., 1996;[172] Trachtenberg and Roehrborn, 1998;[173] Zerbib *et al*., 1994[174]
TUNA vs TURP	4	450	Hill *et al*., 2004;[144] Kim *et al*., 2006;[151] Cimentepe *et al*., 2003;[175] Hindley *et al*., 2001[176]
Stents vs TURP	1	60	Chapple *et al*., 1995[91]
TEAP vs TURP	1	204	Kim *et al*., 2006[151]
Laser coagulation vs TURP	13	1231	Costello *et al*., 1995;[123] Kursh *et al*., 2003;[130] Liedberg *et al*., 2003;[131] Donovan *et al*., 2000;[136] Gujral *et al*., 2000;[139] McAllister *et al*., 2000;[145] Rodrigo Aliaga *et al*., 1998;[149] Kim *et al*., 2006;[151] Chacko *et al*., 2001;[154] Cowles *et al*., 1995;[163] Kabalin *et al*., 1995;[177] Mårtenson *et al*., 1999;[178] Suvakovic and Hindmarsh, 1996[179]
TUIP vs TURP	11	871	Christensen *et al*., 1990;[135] Rodrigo Aliaga *et al*., 1998;[149] Riehmann *et al*., 1995;[152] Hellström *et al*., 1986;[157] Dørflinger *et al*., 1992;[180] Jahnson *et al*., 1998;[181] Li and Ng, 1987;[182] Nielson, 1988;[183] Saporta *et al*., 1996;[184] Soonawalla and Pardanani, 1992;[185] Tkocz and Prajsner, 2002[186]
Laser resection vs TURP	5	530	Kuntz *et al*., 2004;[64] Wilson *et al*., 2006;[134] Gupta *et al*., 2006;[187] Montorsi *et al*., 2004;[188] Westenberg *et al*., 2004[189]
Laser vaporisation vs TURP	11	955	Carter *et al*., 1999;[127] Bouchier-Hayes *et al*., 2006;[141] Shingleton *et al*., 2002;[146] Zorn *et al*., 1999;[148] Tuhkanen *et al*., 2003;[153] Keoghane *et al*., 2000;[164] Suvakovic and Hindmarsh, 1996;[179] Mottet *et al*., 1999;[190] Tuhkanen *et al*., 2001;[191] Sengor *et al*., 1996;[192] van Melick *et al*., 2003[193]
Bipolar TURP vs TURP	6	336	de Sio *et al*., 2006;[65] Singh *et al*., 2005;[147] Kim *et al*., 2006;[150] Seckiner *et al*., 2006;[161] Nuhoğlu *et al*., 2006;[194] Tefekli *et al*., 2005[195]
TUVP vs TURP	17	1449	Kaplan *et al*., 1998;[55] Fowler *et al*., 2005;[57] Erdağı *et al*., 1999;[128] Hammadeh *et al*., 2003;[129] Gallucci *et al*., 1998;[138] Patel *et al*., 1997;[140] Ekengren *et al*., 2000;[142] Gotoh *et al*., 1999;[156] Kupeli *et al*., 1998;[158] Nathan and Wickham, 1996;[162] van Melick *et al*., 2003;[193] Çetinkaya *et al*., 1996;[196] Kupeli *et al*., 1998;[197] Netto *et al*., 1999;[198] Nuhoğlu *et al*., 2005;[199] Shokeir *et al*., 1997;[200] Wang *et al*., 2002[201]
Bipolar TUVP vs TURP	2	211	Hon *et al*., 2006;[70] Dunsmuir *et al*., 2003[137]
TUVRP vs TURP	5	429	Talic *et al*., 2000;[68] Liu *et al*., 2006;[132] Gupta *et al*., 2006;[187] Helke *et al*., 2001;[202] Kupeli *et al*., 2001[203]
Bipolar TUVRP vs TURP	1	60	Fung *et al*., 2005[155]

TEAP, transurethral ethanol ablation of the prostate; TUIP, transurethral incision of the prostate; TUMT, transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TUR, transurethral resection; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate; TUVRP, transurethral vaporesection of the prostate.

Chapter 6

Clinical effectiveness of minimally invasive techniques

Transurethral microwave thermotherapy (TUMT) versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 6*. Six RCTs, reported in 19 papers,[86,124,165–169,207–218] were eligible for this comparison, in which a total of 549 participants were randomised. The number of participants randomised to TUMT or TURP ranged from 2[168] to 99.[165] The total number of participants allocated to TUMT was 314 and the total allocated to TURP was 235.

Two studies each took place in the Netherlands[166,169] and Sweden[167,168] and one in the UK,[124] and one was a multicentre study involving Sweden, Denmark and the US.[165] Only three studies gave details of the recruitment dates;[165,166,169] recruitment dates ranged from January 1994 to November 1999.

Four out of the six RCTs reported baseline IPSS/AUA scores. The total number of participants who had moderate symptoms of BPE and underwent TUMT was 61 (26%), compared with 51 (31%) with moderate symptoms allocated to TURP. There were 177 (74%) patients with severe symptoms in the TUMT group and 112 (69%) with severe symptoms in the TURP group.

Of the studies reporting estimated prostate size, 69 (22%) and 245 (78%) patients allocated to TUMT had moderate-sized and large prostates respectively. Of the patients allocated to TURP, 40 (17%) had moderate-sized and 195 (83%) had large prostates.

TABLE 6 *Summary of the baseline characteristics, TUMT vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Ahmed *et al.*, 1997[124]	TUMT	30	69	18.5	10.1	94	37
	TURP	30	69	18.4	9.5	109	46
Dahlstrand *et al.*, 1993[167]	TUMT	39	68	11.2[b]	8.0	105	33
	TURP	40	70	13.3[b]	7.9	116	37
Dahlstrand *et al.*, 1995[168]	TUMT	37	67	12.1[b]	8.6	194	43[c]
	TURP	32	70	13.6[b]	8.6	1104	45[c]
d'Ancona *et al.*, 1998[166]	TUMT	31	69	18.3	9.3	49	43
	TURP	21	69	16.7	9.3	91	45
de la Rosette *et al.*, 2003[169]	TUMT	78	67	20.0	9.2	65	51
	TURP	66	66	20.0	8.0	91	52
Wagrell *et al.*, 2002[165]	TUMT	99	67	21.0	7.6	106	49
	TURP	46	69	20.4	7.8	94	53

TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate.
Data given as mean values (unless stated otherwise)
a Symptom scores given as IPSS/AUA (unless stated otherwise).
b Prostate length (mm).
c Madsen score.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8. The results of the meta-analyses are given in Appendix 9. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

Of the six eligible studies, three[165,166,213] ($n = 290$) provided information on IPSS/AUA scores (Appendix 8.1, *Table 42*). At 3 months IPSS was higher for TUMT than for TURP (*Figure 3*, comparison 01:01:01). Overall, the WMD was 4.08 (95% CI 2.78–5.39, $p < 0.001$). There was evidence of statistical heterogeneity, but the direction of effect was consistent even though the size of effect estimates varied. Using a random-effects model did not change this pattern. The cause of heterogeneity is unclear but in the study by d'Ancona and colleagues[166] patients appear to have milder disease than in the other two studies.

In total, four studies[166,168,210,213] ($n = 306$) provided information on the improvement of Madsen–Iversen scores after surgery (Appendix 8.1, *Table 42*). Meta-analysis of the four trials showed heterogeneity, with results tending to favour TURP, but the difference was not statistically significant (*Figure 3*, comparison 01:02:01: WMD 0.63, 95% CI –0.08 to 1.33, $p = 0.08$). The direction and size of effect varied across studies, with Dahlstrand and colleagues[168] reporting lower scores for TUMT. This study appears to be contributing much of the statistical heterogeneity that is present and this could be because patients allocated to the TURP group had higher residual volumes. Removal of this study from the analysis resulted in a substantial decrease in heterogeneity.

At 12 months

Meta-analysis of data from three trials[165,166,169] reporting IPSS/AUA scores at 12 months after surgery showed a statistically significant worse score for TUMT compared with TURP (*Figure 3*, comparison 01:01:03: WMD 2.41, 95% CI 1.40–3.42, $p < 0.001$). Again, there was marked statistical heterogeneity between the three studies. When a random-effects model was applied the direction of effect remained the same but the difference between the groups was no longer statistically significant (WMD 2.26, 95% CI –0.38 to 4.91).

At 12 months, all four trials reporting Madsen–Iversen symptom scores[166–168,213] reported higher (worse) scores following TUMT (*Figure 3*, comparison 01:02:03). Overall, the WMD was 1.97 (95% CI 1.27–2.66, $p < 0.001$).

Longer-term follow-up

Two studies reported data beyond 12 months.[166,169] These data also favoured TURP, but again with variation between trials in the estimated size of difference (*Figure 3*, comparison 01:01:05: WMD 8.90, 95% CI 6.65–11.15, $p < 0.001$). A similar trend was observed for the earlier follow-ups.

Complications

Data describing complications are tabulated in Appendix 8.1, *Table 43*. Information on 13 types of complications was identified across the six eligible studies for this comparison. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 4*). Results for other complications are presented in Appendix 9.1, comparison 01:03. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied.

Blood transfusion

Blood transfusion was reported in three studies.[124,166,168] None of the patients required a blood transfusion following TUMT compared with four (5%) patients following TURP (*Figure 4*, comparison 01:03:01: RR 0.11, 95% CI 0.01–1.98, $p = 0.13$).

Urinary retention

In both trials with data,[165,169] urinary retention was reported more commonly in the patients undergoing TUMT than in those undergoing TURP (*Figure 4*, comparison 01:03:02: RR 1.64, 95% CI 0.77–3.50, $p = 0.20$).

Urinary tract infection

Meta-analysis of data from five studies[124,165–168] showed no statistically significant differences between the two arms; the direction of effect varied across studies with two[124,165] favouring TUMT (*Figure 4*, comparison 01:03:03: 16/237 versus 13/174, RR 1.05, 95% CI 0.53–2.08, $p = 0.90$).

Stricture

Only one stricture (urethral) was reported amongst 172 participants allocated to TUMT versus 11 (including five bladder neck stenoses) amongst 168 participants allocated to TURP (*Figure 4*, comparison 01:03:04: RR 0.20, 95% CI 0.05–0.75, $p = 0.02$). The direction and size of effect were consistent across the four studies reporting this outcome. The event rates in this meta-analysis

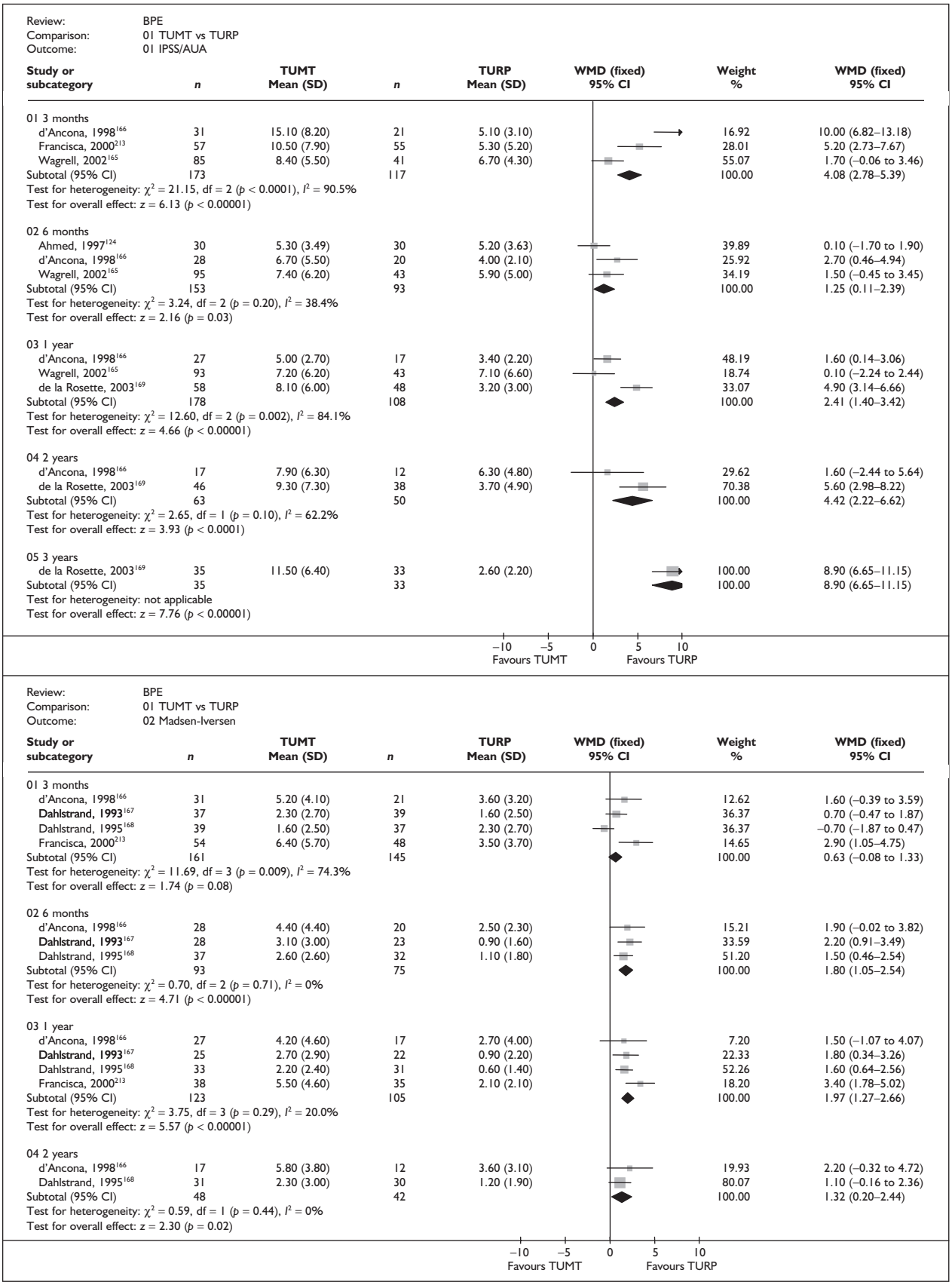


FIGURE 3 *Symptom scores, TUMT vs TURP.*

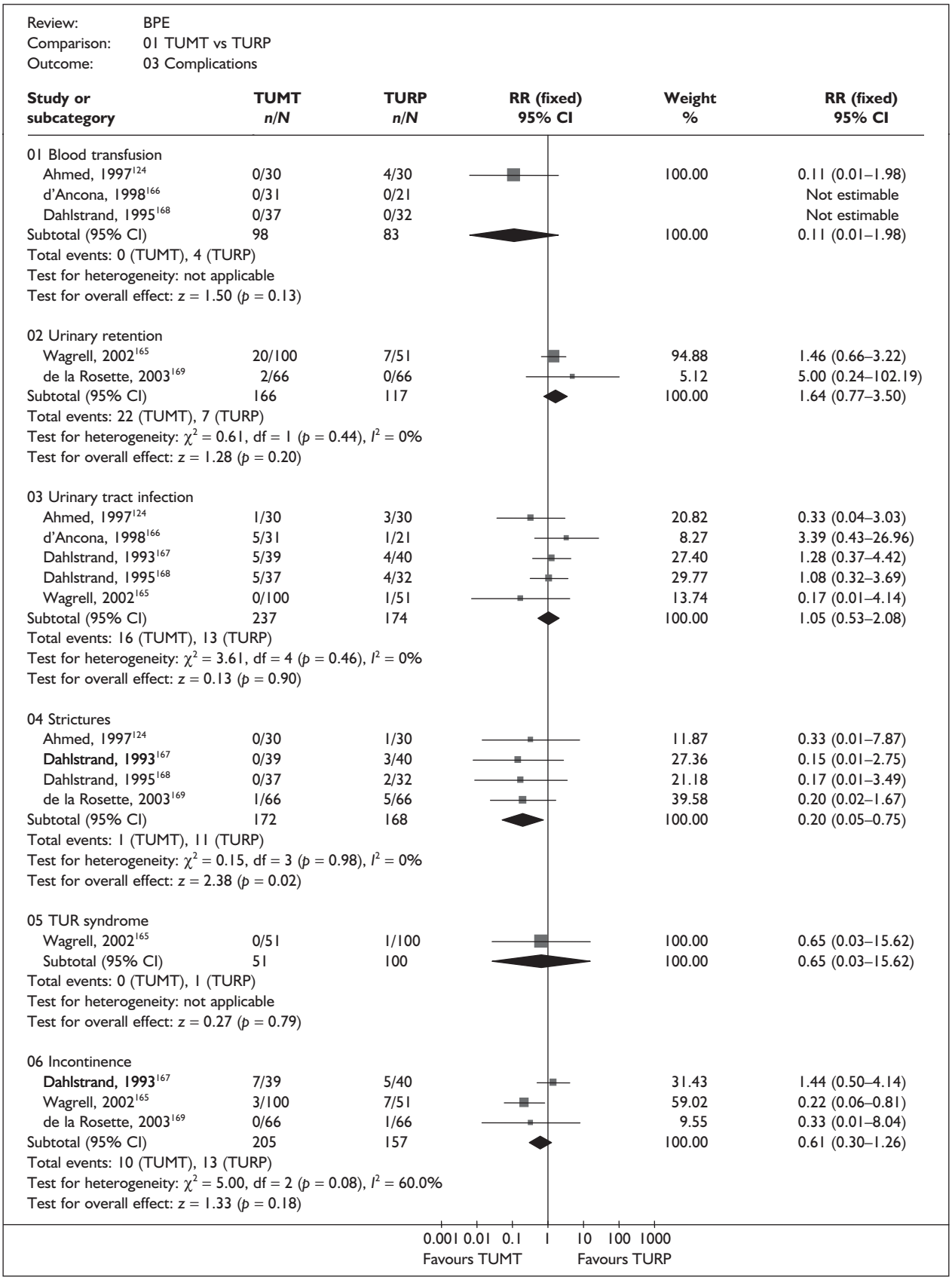


FIGURE 4 *Complications, TUMT vs TURP.*

should be treated with caution as the length of follow-up of the RCTs varied.

TUR syndrome

Out of the six included studies, only one reported data on this outcome.[165] One event was observed in the TURP arm amongst 100 patients as opposed to none in the TUMT arm. This difference does not reach statistical significance, but the confidence intervals were wide and therefore important clinical differences may exist (*Figure 4*, comparison 01:03:05: RR 5.83, 95% CI 0.24–140.55, $p = 0.28$).

Urinary incontinence

A total of 10 (4.9%) people were reported to have incontinence episodes amongst 205 allocated TUMT interventions compared with 13 (8.3%) people amongst 157 allocated TURP interventions (*Figure 4*, comparison 01:03:06: RR 0.61, 95% CI 0.30–1.26, $p = 0.18$). The direction and size of effect varied across studies and there was evidence of statistical heterogeneity across the three studies reporting this outcome.[165,167,169] This may be because some of the studies failed to report the type of incontinence and the length of follow-up varied.

Quality of life

Two studies[165,169] used the IPSS QoL (0–6) questionnaire to measure quality of life of people undergoing TUMT or TURP (Appendix 8.1, *Table 44* and *Figure 5*), where 0 is being delighted and 6 represents feeling terrible concerning urinary symptoms.

At 3 months

Both studies[165,169] reported better quality of life scores at 3 months following TURP. The mean difference based on data from one study[165] was 0.40 for TUMT versus TURP, but this result did not reach statistical significance (*Figure 5*: MD 0.40, 95% CI –0.17 to 0.97, $p = 0.17$).

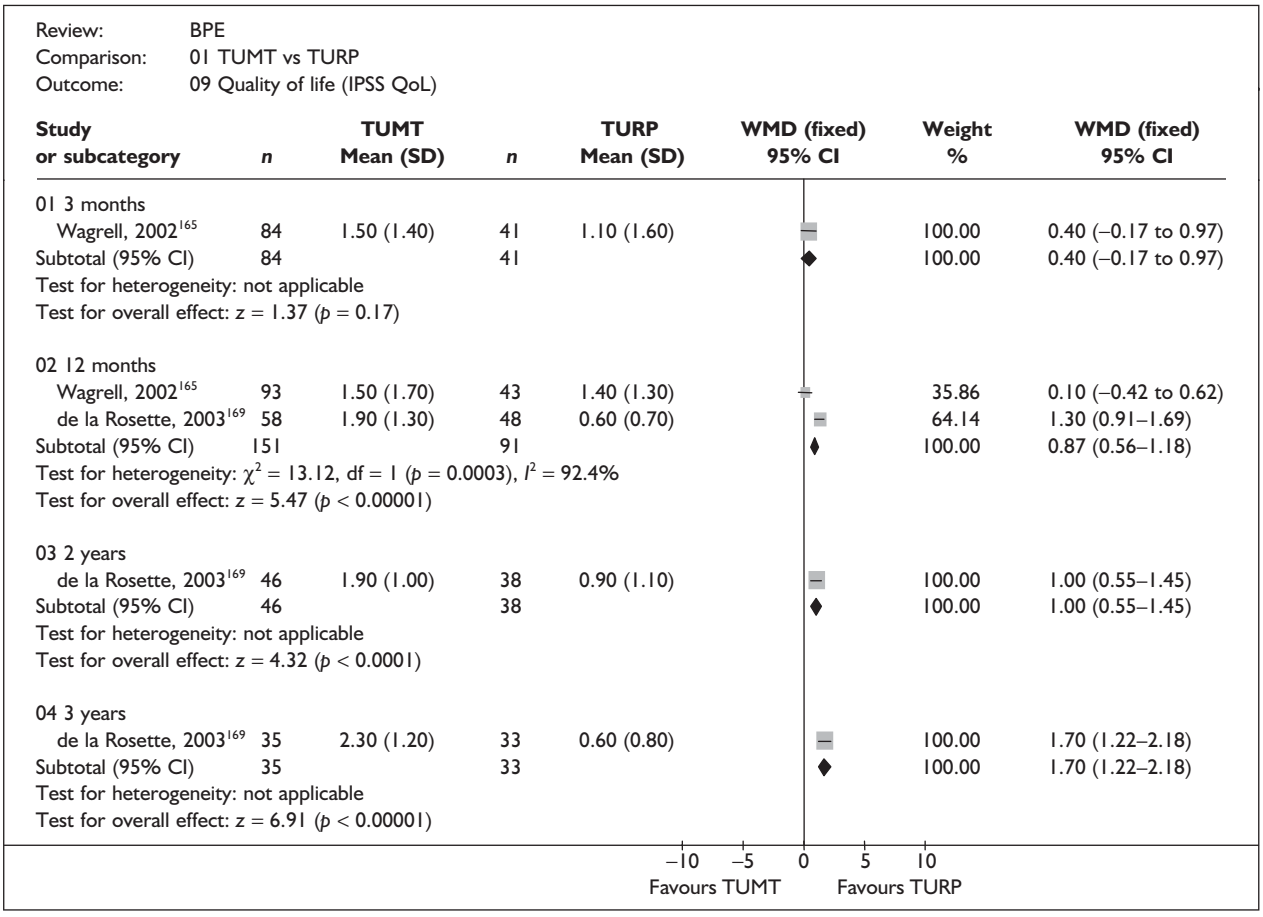


FIGURE 5 *Quality of life, TUMT vs TURP.*

At 12 months

Evidence from the two studies[165,169] showed poorer quality of life scores following TUMT than following TURP (*Figure 5*: WMD 0.87, 95% CI 0.56–1.18, $p < 0.001$). The size of the estimated difference varied but the reasons for this were unclear.

Longer-term follow-up

The mean difference based on data from one study[169] was 1.70 for TUMT versus TURP in terms of quality of life (*Figure 5*: 95% CI 1.22–2.18, $p < 0.001$). However, this same trial gave higher estimates of long-term IPSS/AUA differences than other trials, so the size of the difference in quality of life should be interpreted cautiously.

Urodynamic outcomes

Data on peak urine flow rate, voided volume, residual volume, detrusor pressure and prostate size were reported to a varying extent across the six studies.[124,165–169] Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.1, *Table 45* and Appendix 9.1, comparisons 01:04–01:08.

At all time points considered, the peak urine flow rate was statistically significantly lower in the TUMT arm than in the TURP arm (Appendix 9.1, comparison 01:04); at both 3 and 12 months there was evidence of heterogeneity between studies included in the meta-analyses but there was consistency in the direction of effect. At 3 months, using the random-effects method, the WMD was 5.32 ml/s (95% CI –6.95 to –3.70, $p < 0.001$). The main source of heterogeneity appeared to be from the study by Wagrell and colleagues;[165] however, the reasons for this remain unclear. When data from this study were excluded from the analysis, the trend towards TURP was maintained but the WMD increased (WMD 7.04, 95% CI 4.93–9.15, $p < 0.001$). At 12 months, fitting a random-effects model only increased the imprecision around the estimate of relative effectiveness.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.1, *Table 46*. Information on length of hospital stay and reoperation rates was identified to a varying extent across the six eligible studies for this comparison.

Duration of operation

No studies reported duration of operation.

Length of hospital stay

Length of hospital stay was reported in two studies.[166,169] Note that those allocated to TUMT were treated as outpatients and therefore hospital stay was longer in the TURP arm (Appendix 8.1, *Table 46*; Appendix 9.1, comparison 01:11: WMD 5.30 days, 95% CI 4.48–6.12, $p < 0.001$).

Reoperation

Five studies[124,166–169] provided details on reoperation rates. A total of 22 (10.2%) reoperations were reported amongst 215 participants allocated to TUMT compared with 9 (4.8%) amongst 189 participants allocated to TURP. Meta-analysis of the five trials just failed to reach statistical significance at the conventional 5% level (Appendix 9.1, comparison 01:12: RR 2.01, 95% CI 0.96–4.18, $p = 0.06$). This result should be treated with caution as the length of follow-up of the RCTs varied.

Summary and conclusions of the evidence for and against the intervention

This review considered data from 549 participants across six RCTs of generally moderate to poor quality (or poor reporting). Compared with TURP the data suggest that, after TUMT, improvement in IPSS/AUA symptom scores and quality of life is less, peak urine flow rate is lower, but length of hospital stay is shorter. Data describing blood transfusion, urinary retention, urinary tract infection, stricture, TUR syndrome, urinary incontinence and reoperation rates are too few to provide sufficiently precise estimates of differences but are consistent with fewer complications following TUMT, such as strictures and incontinence.

In this review the results for symptom scores, peak urine flow rate and urinary incontinence displayed statistically significant heterogeneity. Consistency in the direction and size of effect varied in the last outcome. Much of the heterogeneity might be due to differences in the characteristics of participants, particularly differences in prostate size. Moreover, it may in part have been due to differences in power delivery or other technical outputs of surgery across studies and to differences in the way that urinary incontinence is defined. Other likely sources of heterogeneity include differences in the length of follow-up.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for

TABLE 7 *Summary of the clinical effect sizes from meta-analyses, TUMT vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	3 (3)	4.08[a]	2.78–5.39	< 0.001
12 months	3 (3)	2.41[a]	1.40–3.42	< 0.001
Longer term	1 (1)	8.90[a]	6.65–11.15	< 0.001
Madsen–Iversen score				
3 months	4 (4)	0.63[a]	–0.08 to 1.33	0.08
12 months	4 (4)	1.97[a]	1.27–2.66	< 0.001
Longer term	2 (2)	1.32[a]	0.20–2.44	0.02
Blood transfusion	3 (3)	0.11[b]	0.01–1.98	0.13
Urinary retention	2 (2)	1.64[b]	0.77–3.50	0.20
Urinary tract infection	5 (5)	1.05[b]	0.53–2.08	0.90
Stricture	4 (4)	0.20[b]	0.05–0.75	0.02
TUR syndrome	1 (1)	0.65[b]	0.03–15.62	0.28
Incontinence	3 (3)	0.61[b]	0.30–1.26	0.18
Quality of life				
3 months	1 (2)	0.40[a]	–0.17 to 0.97	0.17
12 months	2 (2)	0.87[a]	0.56–1.18	< 0.001
Longer term	1 (1)	1.70[a]	1.22–2.18	< 0.001
Q_{max}				
3 months	4 (4)	–5.35[a]	–7.09 to –3.62	< 0.001
12 months	4 (4)	–5.32[a]	–6.95 to –3.70	< 0.001
Longer term	1 (1)	–11.10[a]	–15.50 to –6.70	< 0.001
Duration of operation	0 (0)	NR	NR	NR
Length of hospital stay	1 (2)	–5.30[a]	–6.12 to –4.48	< 0.001
Reoperation	5 (5)	2.01[b]	0.96–4.18	0.06

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; NR, not reported; TUMT, transurethral microwave thermotherapy; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

which data were available is given in *Table* 7. These should be interpreted in view of the comments mentioned earlier in this section.

Transurethral microwave thermotherapy (TUMT) versus sham

Characteristics of included studies

The baseline characteristics of the included studies are summarised in *Table 8*. A total of 1209 participants were randomised across 11 eligible RCTs reported in 21 papers.[125,126,133,143,159,160,170–174,219–228]

Three studies took place in the US,[126,159,170] three in the UK,[125,133,160] two in France[143,174] and one each in Sweden[171] and the Netherlands,[172] and one was a multicentre trial that took place in the US and Canada.[173] Four studies provided details of recruitment dates;[133,159,160,172] the earliest recruitment date was June 1994 and latest recruitment date was June 1996.

Although all 11 studies gave some details of the ages of participants, three gave only the mean or median age of the participant group as a whole,

TABLE 8 *Summary of the baseline characteristics, TUMT vs sham*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Abbou *et al.*, 1995[143]	TUMT	66	65	10.9[b]	10.4	66	45
	Sham	31	66	12.8[b]	9.9	61	44
Albala *et al.*, 2002[170]	TUMT	125	65	22.5	8.9	58	50
	Sham	65	65	22.7	8.4	53	47
Bdesha *et al.*, 1994[125]	TUMT	22	64	19.2	12.3	104	NR
	Sham	20	63	18.8	10.8	80	NR
Blute *et al.*, 1996[126]	TUMT	78	67	19.9	7.3	140	37.4
	Sham	37	67	20.8	7.4	145	36.1
Brehmer *et al.*, 1999[171]	TUMT 30	14	NR	A/B – 58/40[c]	8.7	NR	≤50
	TUMT 60	16	NR	A/B – 49/36[c]	7.0	NR	≤50
	Sham	14	NR	A/B – 46/36[c]	7.9	NR	≤50
de Wildt *et al.*, 1996[172]	TUMT	46	64	12.9[b]	9.6	85	49
	Sham	47	66	13.7[b]	9.2	94	49
Larson *et al.*, 1998[159]	TUMT	125	66	20.8	7.8	99	38
	Sham	44	66	21.3	7.8	104	45
Nawrocki *et al.*, 1997[160]	TUMT	38	NR	19	8.8	252	86
	Sham	40	NR	17.5	9.4	269	96
Ogden *et al.*, 1993[133]	TUMT	22	68	14.5[b]	8.5	147	38
	Sham	21	67	14.2[b]	8.6	118	35
Trachtenberg and Roehrborn, 1998[173]	TUMT	147	66	23.6	7.7	80	48
	Sham	73	66	23.9	8.1	67	50
Zerbib *et al.*, 1994[174]	TUMT	38	NR	NR	7.6	110	NR
	Sham	30	NR	NR	10.6	84	NR

NR, not reported; TUMT, transurethral microwave thermotherapy.
Data given as mean values (unless stated otherwise).
Symptom scores given as IPSS/AUA (unless stated otherwise).
a Median.
b Madsen score.
c ICS score (32 questions: 'A' question about the actual symptom, 'B' question about the bother related to the symptom; also includes several questions about sexual function; maximum A and B scores 124 and 92 respectively; high score indicates worse symptoms).

regardless of which intervention to which they were randomised.[160,171,174]

Of the studies reporting IPSS/AUA scores at entry, 475 (74%) participants allocated to TUMT had severe symptoms of BPE and 60 (9%) had moderate symptoms. Of the participants randomised to sham, 219 (58%) had severe symptoms and 60 (16%) had moderate symptoms.

Two studies failed to report the prostate size of the enrolled participants[125,174] and in one study authors reported that, to be included, patients had to have prostate sizes of less than 50 ml. The total numbers of participants who had moderate-sized and large prostates in the TUMT group were 225 (34%) and 438 (66%) respectively. The equivalent numbers allocated to a sham procedure were 58 (17%) and 314 (84%) respectively.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.2. The results of the meta-analyses are given in Appendix 9.2. Because of the nature of the comparator intervention (sham), the most useful information comes from short-term outcomes. The value of long-term assessment of outcomes is limited by a high dropout rate as most of the patients were judged to require a true TUMT procedure by 12 months; it is likely that only the least severe patients at baseline remained untreated at this time point, thus comparisons limited to untreated men are subject to selection bias.

Symptom scores

At 3 months

Of the 11 eligible studies, eight provided information on symptom scores at 3 months following surgery.[125,126,133,159,160,170,172,173] Six of those reported IPSS/AUA scores.[125,126,159,160,170,173] In all studies, IPSS/AUA scores were superior in the TUMT group and this was statistically significant in all six studies ($p < 0.05$). Only three studies[125,126,159] presented data in a form that was sufficiently similar to allow quantitative synthesis (*Figure 6*, comparison 02:01:01). The WMD was –5.69 (95% CI –7.38 to –3.99, $p < 0.00001$) for TUMT versus sham surgery. This result is consistent with the data from those trials that provided data that were not amenable for meta-analysis.

Meta-analysis of three studies reporting Madsen–Iversen scores[126,133,172] showed that TUMT resulted in a greater decrease in score than sham treatment (*Figure 6*, comparison 02:02:01: WMD –5.66, 95% CI –6.85 to –4.46, $p < 0.000001$). There was some evidence of heterogeneity and, when a random-effects model was fitted, the principal change was in the width of the confidence interval. The main source of heterogeneity appeared to be the study by Ogden and colleagues;[133] however, the reasons for this are unclear. When data from Ogden and colleagues were removed from the analysis, the trend towards TUMT was maintained but the WMD decreased (WMD –5.10, 95% CI –6.40 to –3.79, $p < 0.00001$).

At 12 months

No studies reported IPSS/AUA symptom scores for patients at 12 months after the surgery.

One study reported Madsen–Iversen symptom scores at 12 months following surgery.[172] The WMD was –4.00 (*Figure 6*, comparison 02:02:03: 95% CI –5.81 to –2.19, $p < 0.0001$).

Longer-term follow-up

No longer-term follow-up data on symptom scores have been reported by any of the eligible studies.

Complications

Data describing complications by study are detailed in Appendix 8.2, *Table 48*. Out of the eligible studies, complications were reported in ten.[125,126,133,143,159,160,170–173] Ten categories of complications were identified. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures and urinary incontinence are presented in this section (*Figure 7*). Results for other complications are presented in Appendix 9.2, comparison 02:03. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied.

Blood transfusion

Only one study[159] provided details on blood transfusion rates. There were no reports of blood transfusions amongst 125 and 44 patients allocated to TUMT or sham respectively.

Urinary retention

All seven trials with data showed higher rates of urinary retention after TUMT. This applied to a total of 77 (12%) patients amongst 644 allocated to TUMT compared with two (0.5%) amongst 360 patients allocated to a sham procedure (*Figure 7*, comparison 02:03:02: RR 10.57, 95% CI 4.11–27.20, $p < 0.0001$). This result should be treated with caution as the length of follow-up of the RCTs varied.

Urinary tract infection

Meta-analysis of data from four trials[133,143,159,173] that reported urinary tract infections showed a higher number of infections following TUMT; however, this was not statistically significant (*Figure 7*, comparison 02:03:03: RR 1.49, 95% CI 0.84–2.67, $p = 0.17$).

Stricture

Urethral strictures were reported in two trials.[159,170] Three cases were reported in one trial following TUMT, with no cases following sham treatment (*Figure 7*, comparison 02:03:04: 3/246 versus 0/106, RR 2.50, 95% CI 0.13–47.46, $p = 0.54$).

Incontinence

Data on incontinence from one trial[159] showed five cases (4%) out of a total of 125 patients following TUMT versus no cases after sham treatment. This result was not statistically significant and confidence intervals were wide (*Figure 7*,

Review: BPE
Comparison: 02 TUMT vs sham
Outcome: 01 IPSS/AUA

Study or subcategory	n	TUMT Mean (SD)	n	Sham Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Bdesha, 1994[125]	22	7.10 (5.00)	18	16.20 (7.35)		18.00	−9.10 (−13.09 to −5.11)
Blute, 1996[126]	64	11.30 (6.30)	31	16.30 (7.60)		30.00	−5.00 (−8.09 to −1.91)
Larson, 1998[159]	123	9.60 (5.94)	40	14.50 (6.77)		52.00	−4.90 (−7.25 to −2.55)
Subtotal (95% CI)	209		89			100.00	−5.69 (−7.38 to −3.99)
Test for heterogeneity: $\chi^2 = 3.44$, df = 2 ($p = 0.18$), $I^2 = 41.8\%$							
Test for overall effect: $z = 6.59$ ($p < 0.00001$)							
02 6 months							
Larson, 1998[159]	120	10.50 (7.26)	35	14.30 (6.34)		100.00	−3.80 (−6.27 to −1.33)
Subtotal (95% CI)	120		35			100.00	−3.80 (−6.27 to −1.33)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 3.02$ ($p = 0.003$)							

−10 −5 0 5 10
Favours TUMT Favours sham

Review: BPE
Comparison: 02 TUMT vs sham
Outcome: 02 Madsen-Iversen

Study or subcategory	n	TUMT Mean (SD)	n	Sham Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Blute, 1996[126]	75	6.30 (5.00)	35	10.80 (4.40)		41.86	−4.50 (−6.35 to −2.65)
Ogden, 1993[133]	21	4.30 (4.44)	19	12.80 (5.00)		16.46	−8.50 (−11.44 to −5.56)
de Wildt, 1996[172]	45	4.70 (3.93)	43	10.40 (4.85)		41.68	−5.70 (−7.55 to −3.85)
Subtotal (95% CI)	141		97			100.00	−5.66 (−6.85 to −4.46)
Test for heterogeneity: $\chi^2 = 5.10$, df = 2 ($p = 0.08$), $I^2 = 60.8\%$							
Test for overall effect: $z = 9.29$ ($p < 0.00001$)							
02 6 months							
de la Rosette, 1994[223]	24	5.30 (4.40)	23	9.10 (4.31)		100.00	−3.80 (−6.29 to −1.31)
Subtotal (95% CI)	24		23			100.00	−3.80 (−6.29 to −1.31)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 2.99$ ($p = 0.003$)							
03 12 months							
de Wildt, 1996[172]	33	4.20 (3.37)	13	8.20 (2.57)		100.00	−4.00 (−5.81 to −2.19)
Subtotal (95% CI)	33		13			100.00	−4.00 (−5.81 to −2.19)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 4.33$ ($p < 0.0001$)							

−10 −5 0 5 10
Favours TUMT Favours sham

FIGURE 6 *Symptom scores, TUMT vs sham.*

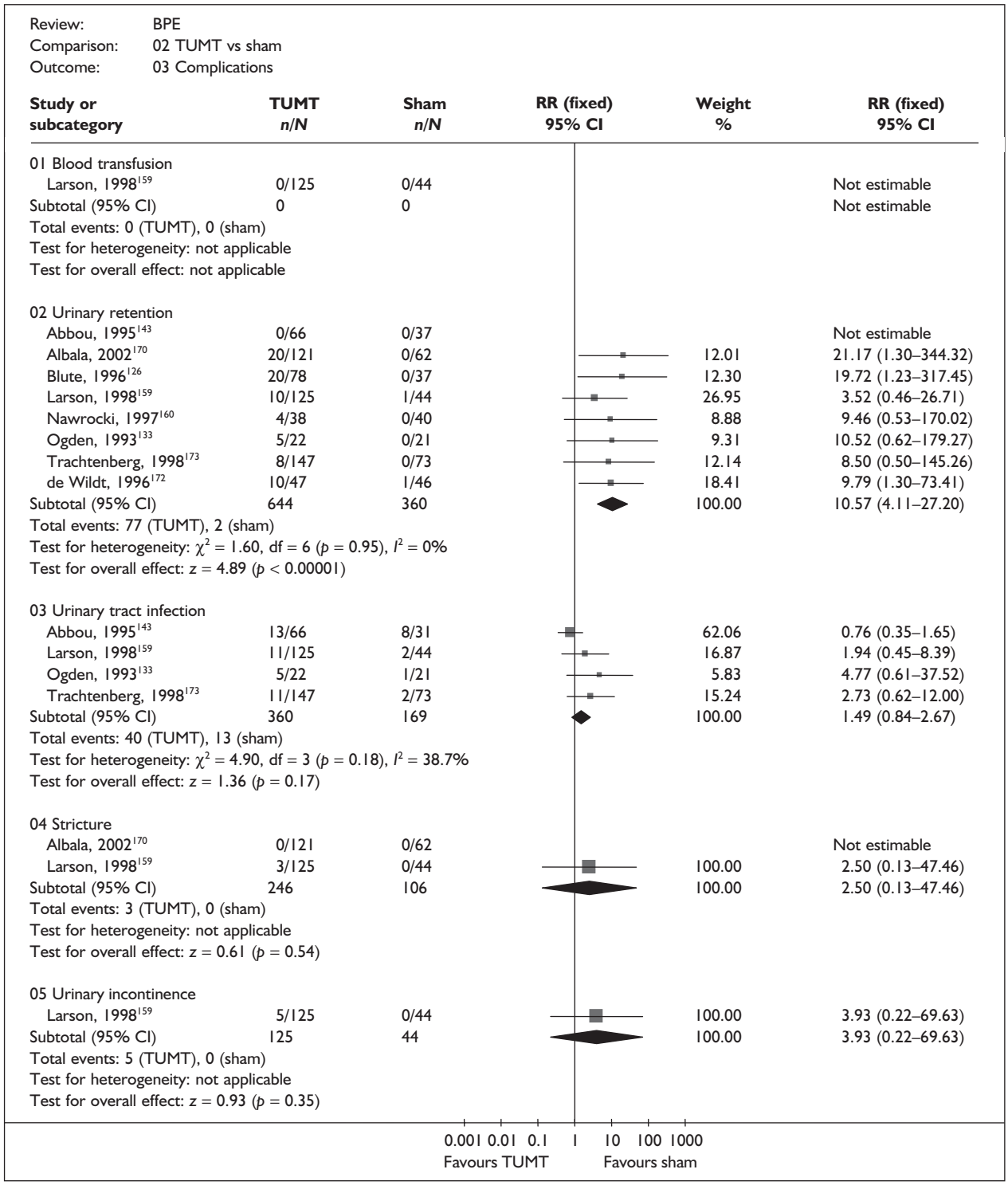


FIGURE 7 *Complications, TUMT vs sham.*

comparison 02:03:05: RR 3.93, 95% CI 0.22–69.63, $p = 0.35$).

Quality of life

Four studies,[133,159,170,173] using a variety of instruments, reported the quality of life of people undergoing TUMT or a sham procedure (Appendix 8.2, *Table 49*). In two studies[159,173] the quality of life was assessed using the IPSS QoL (0–6) questionnaire. This was evaluated by patients' responses to the question of how they would feel if their current urinary symptoms were to continue indefinitely. In the third study[170] quality of life index was used and in the final study[133] quality of life was measured using a questionnaire derived from the Veterans' Administration study of TURP versus watchful waiting. This questionnaire had five sections: A, perception of urinary difficulties; B, sexual performance; C, activities of daily living; D, general psychological well-being; and E, social activities. At the 3-month evaluation, two studies[133,173] reported higher quality of life following TUMT. This difference was statistically significant in both studies ($p < 0.05$). Larson and colleagues[159] report that the improvement in quality of life score remained at a comparable level in the 12-month evaluation in the TUMT group.

Urodynamic outcomes

Data on peak urine flow rate, voided volume and residual volume were reported across 11 studies.[125,126,133,143,159,160,170–174] Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.2, *Table 50* and Appendix 9.2, comparisons 02:04–02:09.

A total of seven studies[125,126,133,159,172–174] reported peak urine flow rate at 3 months after surgery. In all but one study[174] the peak urine flow rate was higher in the TUMT group. Six studies[125,126,133,159,172,174] presented data that were sufficiently similar to allow quantitative synthesis (Appendix 9.2, comparison 02:04:01: WMD 2.53 ml/s, 95% CI 1.69–3.37, $p < 0.001$). With regard to longer-term follow-up (12 months), only one study[172] reported this outcome (WMD 2.90, 95% CI –0.24 to 6.04, $p = 0.07$).

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.2, *Table 51*. Information on reoperation rates was identified in five studies.

Duration of operation

No studies reported this outcome.

Length of hospital stay

No studies reported this outcome.

Reoperation

The percentage of patients requiring a reoperation in the TUMT group was 6% compared with 54% of patients in the sham group requiring surgery. Meta-analysis of five trials[125,133,159,171,172] presents a RR of 0.14 in favour of TUMT (95% CI 0.09–0.23, $p < 0.00001$).[37,46,69,80,81] This result should be interpreted with caution as the length of follow-up varied.

Summary and conclusions of the evidence for and against the intervention

This review considered data from 1209 participants across 11 RCTs of generally moderate to poor quality (with respect to conduct and reporting). The data suggest that TUMT both reduces symptoms and increases peak urine flow rate at 3 months after the procedure. Reoperation rates for TUMT were lower than for sham. Patients who underwent TUMT had a high risk of developing urinary retention. Confidence intervals were wide. The meta-analyses failed to indicate differences in the incidence of blood transfusion, strictures and urinary incontinence, although the direction of effect was consistent with what would be expected after an operative procedure, again with wide confidence intervals.

In this review the data contributing to meta-analyses were too few to provide precise estimates of differences, particularly for the complications, and confidence intervals were so wide that clinically important differences could not be ruled out.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 9*. Again, these should be interpreted in view of the comments mentioned above.

TABLE 9 *Summary of the clinical effect sizes from meta-analyses, TUMT vs sham*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	3 (6)	–5.69[a]	–7.38 to –3.99	< 0.001
12 months	0 (1)	NR	NR	NR
Longer term	0 (0)	NR	NR	NR
Madsen–Iversen score				
3 months	3 (4)	–5.66[a]	–6.85 to –4.46	< 0.001
12 months	1 (3)	–4.00[a]	–5.81 to –2.19	< 0.001
Longer term	0 (0)	NR	NR	NR
Blood transfusion	1 (1)	NE	NE	NE
Urinary retention	8 (8)	9.12[b]	3.36–24.80	< 0.001
Urinary tract infection	4 (4)	1.49[b]	0.84–2.67	0.17
TUR syndrome	0 (0)	NR	NR	NR
Stricture	2 (2)	2.50[b]	0.13–47.46	0.54
Incontinence	1 (1)	3.93[b]	0.22–69.63	0.35
Quality of life				
3 months	0 (2)	NR	NR	NR
12 months	0 (0)	NR	NR	NR
Longer term				
Q_{max}				
3 months	6 (9)	2.53[a]	1.69–3.37	< 0.001
12 months	1 (4)	2.90[a]	–0.24 to 6.04	0.07
Longer term	0 (0)	NR	NR	NR
Duration of operation	0 (0)	NR	NR	NR
Length of stay	0 (0)	NR	NR	NR
Reoperation	5 (5)	0.14[b]	0.09–0.23	< 0.001

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; NR, not reported; TUMT, transurethral microwave thermotherapy; TUR, transurethral resection.
a Weighted mean difference.
b Relative risk.

Transurethral needle ablation (TUNA) versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 10*. Four RCTs, reported in nine papers,[144,151,175,176,229–233] were eligible for this comparison, in which a total of 450 participants were randomised. These trials took place in the US,[144] Turkey,[175] Korea[151] and the UK.[176]

All four studies provided details of the participants' baseline IPSS/AUA symptom scores, according to which all 450 participants had severe symptoms.

The studies presented variations in relation to prostate size. Of the studies reporting this characteristic, 65 (32%) and 136 (66%) participants randomised to TUNA had moderate-sized and large prostates respectively. Of the patients allocated to TURP, 56 (28%) had moderate-sized prostates and 143 (72%) had large prostates.

TABLE 10 *Summary of the baseline characteristics, TUNA vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Cimentepe *et al.*, 2003[175]	TUNA	26	60	22.9	9.8	67	46
	TURP	33	63	24.1	9.2	76	49
Hill *et al.*, 2004[144]	TUNA	65	66	23.9	8.8	92	36
	TURP	56	66	24.1	8.8	83	36
Hindley *et al.*, 2001[176]	TUNA	25	66[b]	22[b]	8.5	55	NR
	TURP	25	71[b]	20[b]	9.0	74	NR
Kim *et al.*, 2006[151]	TUNA	110	66	20.8	7.0	257	41
	TURP	110	67	24.0	11.9	187	44

NR, not reported; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate.
Data given as mean values (unless stated otherwise).
a Symptom scores given as IPSS/AUA.
b Median.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.3. The results of the meta-analyses are given in Appendix 9.3. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

At 3 months after surgery, three out of the four eligible trials reported AUA/IPSS symptom scores.[144,151,175] Only two studies reported data that were amenable to meta-analysis.[144,175] Symptom scores were slightly lower following TURP than following TUNA (*Figure 8*, comparison 03:01:01: WMD 1.18, 95% CI –0.03 to 2.40, $p = 0.06$).

At 12 months

Three reports presented IPSS/AUA results at 12 months of follow-up.[144,151,176] Analysis of data from one report showed better symptom scores in patients undergoing TURP than in those following TUNA (*Figure 8* comparison 03:01:03: MD 3.90, 95% CI 1.27–6.53, $p = 0.004$). This result is consistent with that observed in the studies by Hindley and colleagues[176] and Kim and colleagues.[151]

Longer-term follow-up

Only one trial[144] reported 5-year IPSS/AUA scores. At this point in time, TUNA and TURP appeared to be equivalent in terms of improvement in symptoms, albeit with confidence intervals that included differences seen at earlier time points (*Figure 8* comparison 03:01:07: MD 0.60, 95% CI –3.55 to 4.75, $p = 0.78$). The narrowing of the difference reflected better scores in the TUNA group. This should be interpreted cautiously as this follow-up included 33% of those who initially underwent surgery and so could reflect selection bias.

Data for other follow-up times (2 and 3 years) were also reported by Hill and colleagues[144] and can be seen in Appendix 8.3, *Table 52* and the respective forest plots in *Figure 8*.

Complications

Data describing complications are tabulated in Appendix 8.3, *Table 53*. Information on nine categories of complications was identified across the four eligible studies for this comparison. The data were too few to provide precise estimates of differences and all confidence intervals were wide such that clinically important differences could not be ruled out. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures and urinary incontinence are presented in this section (*Figure 9*). Results for other complications are presented in Appendix 9.3, comparison 03:03. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied. Also, for urinary incontinence it was unclear whether the type of incontinence considered was the same across all studies.

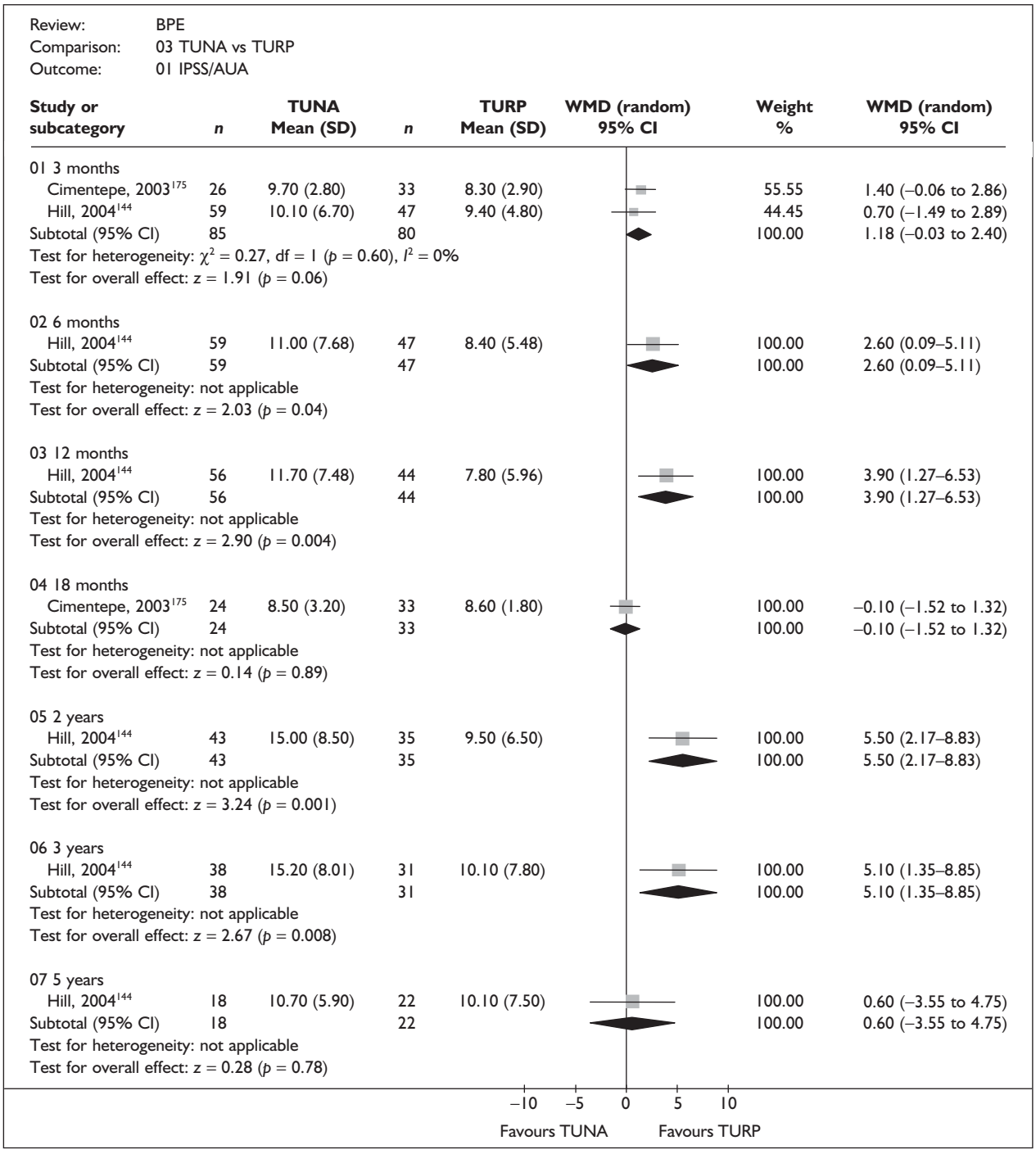


FIGURE 8 *Symptom scores, TUNA vs TURP*

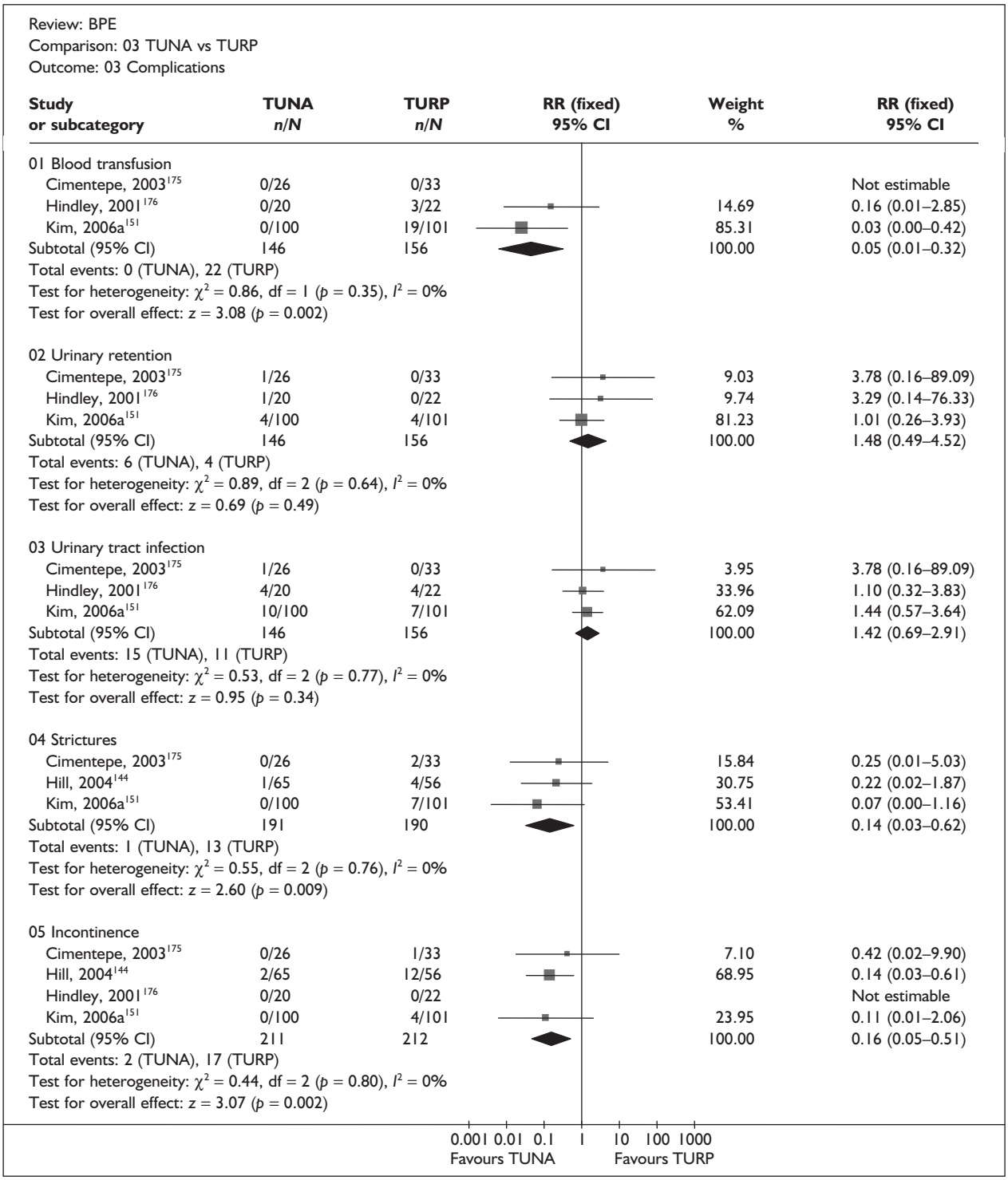


FIGURE 9 *Complications, TUNA vs TURP.*

Blood transfusion

There were no cases of blood transfusion in the TUNA arms amongst 146 patients across three studies.[144,151,175] Blood transfusion was required in 14% ($n = 22$) of the patients undergoing TURP (*Figure 9*, comparison 03:03:01: RR 0.05, 95% CI 0.01–0.32, $p = 0.002$).

Urinary retention

Urinary retention following surgery was reported in three studies.[151,175,176] Six cases (4.1%) of urinary retention were recorded amongst 146 patients in the TUNA arms. Four patients (2.6%) who underwent TURP exhibited urinary retention. The confidence intervals are wide and, therefore, this result should be interpreted with caution (*Figure 9*, comparison 03:03:02: RR 1.48, 95% CI 0.49–4.52, $p = 0.49$).

Urinary tract infection

Urinary tract infection occurred more frequently in the TUNA arms (10.2%) than in the TURP arms (7.0%), but again with wide confidence intervals (*Figure 9*, comparison 03:03:03 RR 1.42, 95% CI 0.69–2.91, $p = 0.34$).

Stricture

Across three trials, the incidence of strictures or bladder neck contractures was documented in one patient (0.5%) in the TUNA group and 13 (6.8%) in the TURP group. This difference was statistically significant (*Figure 9*, comparison 03:04: RR 0.14, 95% CI 0.03–0.62, $p = 0.009$).

TUR syndrome

No studies reported this outcome.

Urinary incontinence

All four studies reported urinary incontinence following surgery. The types of incontinence were not fully described across studies (Appendix 8.3, *Table 53*). The overall incidence of urinary incontinence was 0.9% ($n = 2$) in the TUNA group versus 8.0% ($n = 17$) in the TURP group (*Figure 9*, comparison 03:03:05: RR 0.16 95% CI 0.05–0.51, $p = 0.002$).

Quality of life

Four studies,[144,151,175,176] using a variety of instruments, reported the quality of life of people following TUNA or TURP (Appendix 8.3, *Table 54*). In three studies[151,175,176] the quality of life was assessed using the IPSS QoL (0–6) questionnaire. In one study[144] the type of scale used to measure quality of life was unclear.

At 3 months

Two studies[151,175] provided details on quality of life at 3 months after surgery. Only one study[175] provided data that were amenable to meta-analysis. Quality of life was higher for TURP with a mean difference of 0.20 (95% CI –0.10 to 0.50, $p = 0.19$). This result was not statistically significant (*Figure 10*, comparison 03:08:01). This result should be treated with caution as the total number of participants available for this evaluation was unclear. This result is, however, consistent with that provided by Kim and colleagues.[151]

At 12 months

Three studies[144,151,176] provided details on quality of life at 12 months after surgery; however, only one was suitable for quantitative synthesis. The quality of life was higher for TURP with a WMD of 0.60 (*Figure 10*, comparison 03:08:02: 95% CI –1.08 to 2.28, $p = 0.48$). This result is consistent with those reported by Hindley and colleagues[176] and Kim and colleagues.[151]

Longer-term follow-up

Evidence from one study[144] indicated that the quality of life of patients who underwent both TUNA and TURP decreased over time; however, it remained statistically significantly better compared with quality of life measured at baseline ($p < 0.0001$). Up to 5 years the two procedures appear to be comparable in terms of quality of life (*Figure 10*, comparison 03:08:03–03:08:07). The loss to follow-up is high and caution should be taken when interpreting the results of this meta-analysis.

Urodynamic outcomes

Data on peak urine flow rate, residual volume, detrusor pressure and prostate size were reported to a varying extent across four studies.[144,151,175,176] These are tabulated in Appendix 8.3, *Table 55*. Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.3, *Table 55* and Appendix 9.3, comparisons 03:04–03:07.

Peak urine flow rate was statistically significantly lower in the TUNA arm than in the TURP arm at all time points (Appendix 9.3, comparison 03:04). At 12 months there was evidence of statistical heterogeneity in the results; however, the direction of effect is consistent across the two studies reporting data amenable to meta-analysis[144,176] and with the results reported by Kim and colleagues.[151] Applying a random-effects model did not change

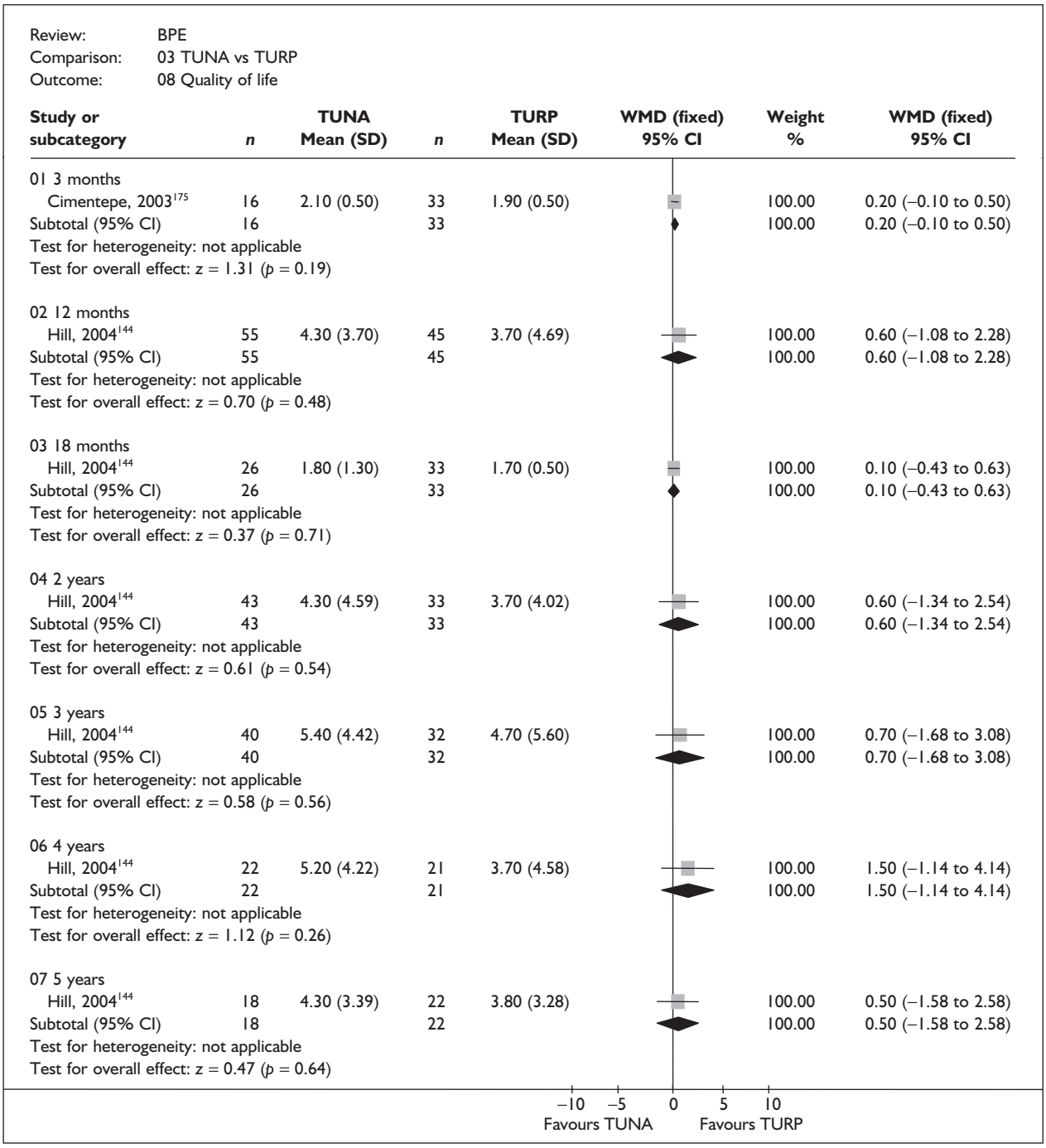


FIGURE 10 *Quality of life, TUNA vs TURP.*

this pattern. The total number of patients contributing to the measurement of this estimate is unclear and it should be noted that only 20% and 27% of those who underwent TUNA and TURP, respectively, were available for the 5-year follow-up assessment. Thus, these results should be treated with considerable caution.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.3, *Table 56*. Information on duration of operation, length of hospital stay and reoperation rates was identified to a varying extent across the three eligible studies for this comparison.

Duration of operation

Two studies[151,175] provided information on the duration of operation (Appendix 8.3, *Table 56*). Only one study provided data that were suitable for quantitative synthesis. The duration of operation in the TUNA group was on average 11.60 minutes longer than the duration of operation in the TURP group (Appendix 9.3, comparison 03:09: 95% CI 6.41–16.79, $p < 0.001$). This result was consistent with that reported by Kim and colleagues[151] who reported that TUNA took 14 minutes more than TURP.

Length of hospital stay

Length of hospital stay appeared to be longer for patients undergoing TUNA than for those undergoing TURP in two studies. Hindley and colleagues[176] reported that patients undergoing TUNA are discharged a few days following the procedure whereas patients undergoing TURP are discharged in the first postoperative day. Cimentepe and colleagues[175] treated TURP patients as outpatients whereas patients allocated to TUNA would stay for at least 48 hours. On the other hand, Kim and colleagues[151] reported a shorter length of hospital stay for those patients undergoing TUNA, with a mean difference of 5.2 days.

Reoperation

Across the four trials, reoperations were documented in 6.2% (13/211) of patients allocated to TUNA compared with 0.5% (1/212) of patients in the TURP group (RR 6.89, 95% CI 1.58–29.95). Although the difference is statistically significant, the confidence interval is wide and it should be noted that the follow-up of the three eligible studies varied from 12 months[144,151] to 2 years.[176]

Summary and conclusions of the evidence for and against the intervention

This review considered data from four RCTs of moderate quality. A total of 450 participants were randomised across the four studies and therefore the data were too few to provide precise estimates for all of the outcomes. A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 11*.

Stents versus transurethral resection of the prostate (TURP)

Characteristics of included studies

No full-text reports of RCTs were identified in the searches. One abstract of an RCT presented as a conference proceeding was identified.[91] This UK study allocated 34 men to undergo prostatic stent insertion and 26 to undergo TURP.

The mean age of participants allocated to stent insertion was 73 years (range 63–86) compared with 72.6 years (range 63–86) for patients allocated to TURP.

On average, participants in the TURP arm had more severe symptoms (mean = 21.6) than those in the stents arm (mean = 19.0).

Participants in both arms presented equivalent mean peak urine flow rate measurements of 8.0 ml/s.

Assessment of effectiveness

Symptom scores

At 3 months

The mean IPSS scores observed at 3 months were 11.2 and 11.0 in the stents and TURP groups respectively.

Complications

The stents group exhibited a slight increase in irritative urinary symptoms compared with the TURP group.

Urodynamic outcomes

The only uroflowmetry data reported were peak urine flow rate. There was no statistically significant difference between the use of a Urolume stent and TURP (MD 0.00, 95% CI –5.84 to 5.84, $p = 1.00$).

Descriptors of care

The only descriptor of care observed was two reoperations in the stents group because of misplacement of the Urolume stent. The authors describe this as being due to technical reasons and therefore a TURP procedure was carried out.

TABLE 11 *Summary of the clinical effect sizes from meta-analyses, TUNA vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	2 (3)	1.18[a]	–0.03 to 2.40	0.06
12 months	1 (3)	3.90[a]	1.27–6.53	0.004
Longer term	1 (1)	0.60[a]	–3.55 to 4.75	0.78
Blood transfusion	3 (3)	0.05[b]	0.01–0.32	0.002
Urinary retention	3 (3)	1.48[b]	0.49–4.52	0.49
Urinary tract infection	3 (3)	1.42[b]	0.69–2.91	0.34
Stricture	3 (3)	0.14[b]	0.03–0.62	0.009
TUR syndrome	0 (0)	NR	NR	NR
Incontinence	4 (4)	0.16[b]	0.05–0.51	0.002
Quality of life				
3 months	1 (2)	0.20[a]	–0.10 to 0.50	0.19
12 months	1 (3)	0.60[a]	–1.08 to 2.28	0.48
Longer term	1 (1)	0.50[a]	–1.58 to 2.58	0.64
Q_{max}				
3 months	1 (2)	–6.40[a]	–8.90 to –3.90	< 0.001
12 months	2 (3)	–8.12[a]	–10.85 to –5.40	< 0.001
Longer term	1 (1)	–7.20[a]	–12.28 to –2.12	0.005
Duration of operation	1 (2)	11.60[a]	6.41–16.79	< 0.001
Length of hospital stay	0 (3)	NR	NR	NR
Reoperation	4 (4)	6.89[b]	1.58–29.95	0.01

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; NR, not reported; TUNA, transurethral needle ablation; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

Transurethral ethanol ablation of the prostate (TEAP) versus TURP

Characteristics of included studies

One RCT was identified.[151] In this Korean study, 94 men were allocated to undergo TEAP and 110 to undergo TURP.

The mean age of participants allocated to TEAP was 66 years (range 49–88) compared with 67 years (range 60–87) for patients allocated to TURP.

All participants had severe symptoms and the mean or median peak urine flow rate measurements were 7.2 and 11.9 ml/s for the TEAP and TURP groups respectively. All participants in the TEAP arm had moderate-sized prostates whereas those in the TURP arm had large prostates.

Assessment of effectiveness

Symptom scores

The mean IPSS scores observed at 3 months were 9.6 and 10.6 in the TEAP and TURP groups respectively. The mean difference was similar at 12 months with scores of 7.5 for TEAP and 8.8 for TURP.

Complications

Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 11*). These results should be treated with caution as the time points at which the complications took place were uncertain.

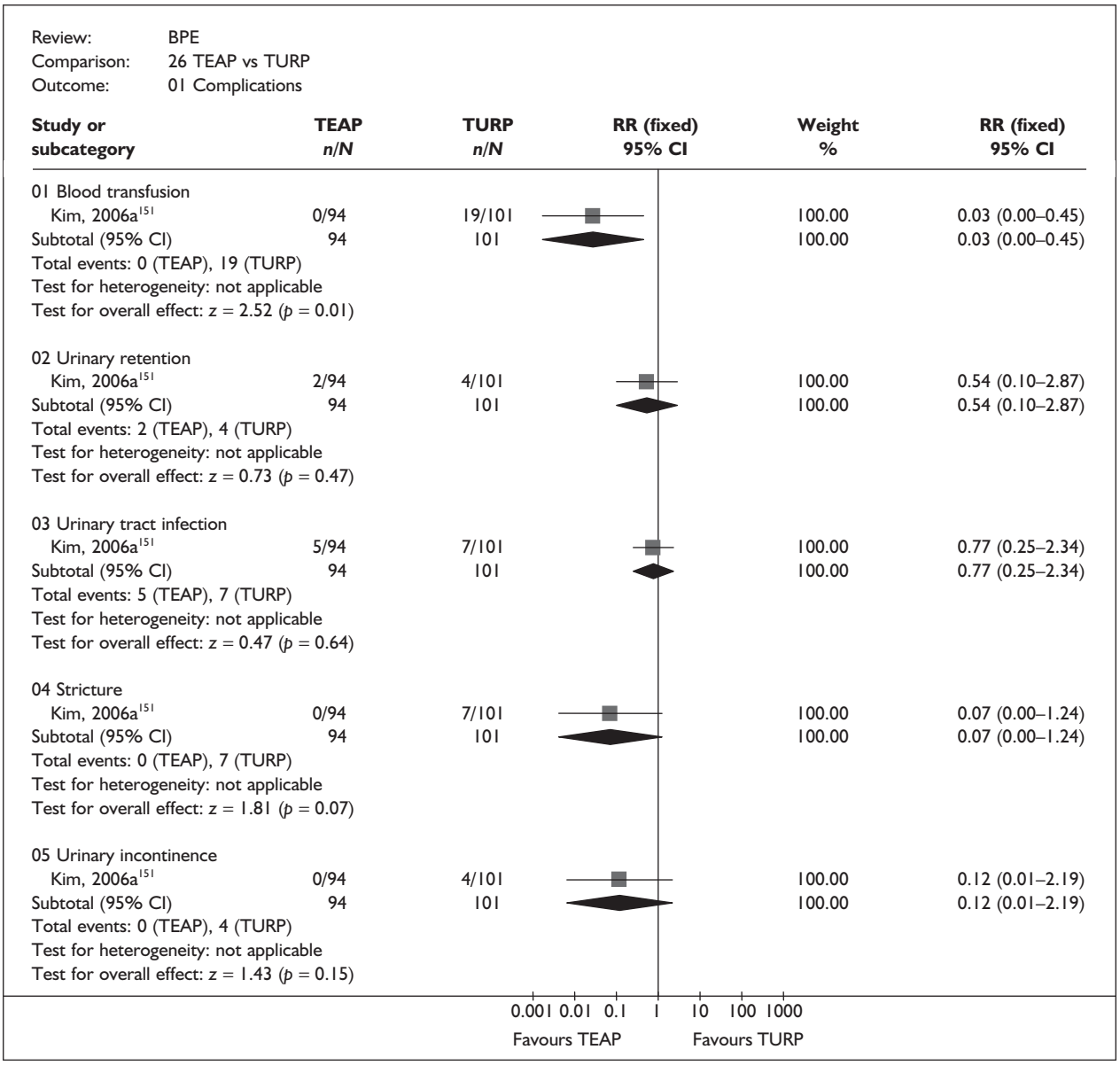


FIGURE 11 *Complications, TEAP vs TURP*

Blood transfusion

There were no blood transfusions reported across 94 patients in the TEAP arm compared with 19 (19%) reported in the TURP arm (*Figure 11*, comparison 26:01:01: RR 0.03, 95% CI 0.00–0.45, $p = 0.01$).

Urinary retention

Two cases (2%) of urinary retention were reported amongst the 94 patients allocated to TEAP compared with four cases (4%) across 101 patients allocated to TURP. This difference was not statistically significant (*Figure 11*, comparison 26:01:02: RR 0.54, 95% CI 0.10–2.87, $p = 0.47$).

Urinary tract infection

No statistically significant difference was observed between the two arms in terms of urinary tract infections (*Figure 11*, comparison 26:01:03: RR 0.77, 95% CI 0.25–2.34, $p = 0.64$).

Stricture

There were no cases of strictures or bladder neck stenosis in the TEAP arm as opposed to seven cases (7%) in the TURP arm. This result did not reach statistical significance (*Figure 11*, comparison 26:01:04: RR 0.07, 95% CI 0.00–1.24, $p = 0.07$).

Urinary incontinence

Urinary incontinence was observed in four patients following TURP amongst a total of 101 randomised patients. Again, this result did not reach statistical significance (*Figure 11*, comparison 26:01:05: RR 0.12, 95% CI 0.01–2.19, $p = 0.15$).

Quality of life

Quality of life was measured in terms of IPSS QoL scores and was found to be improved in both arms at both the 3- and 12-month assessments. Quality of life measurements at 3 and 12 months following surgery were 3.4 and 2.3, respectively, for those in the TEAP arm compared with 2.8 and 2.6, respectively, for those in the TURP arm.

Urodynamic outcomes

Mean differences in peak urine flow rates at 3 and 12 months were approximately 7.9 ml/s in favour of TURP.

Descriptors of care

Duration of operation and length of hospital stay were shorter in the TEAP arm than in the TURP arm. No reoperations were recorded in either arm.

Laser coagulation versus TURP

Laser coagulation of the prostate is a method that encompasses several techniques including interstitial laser coagulation, visual laser ablation and transurethral laser prostatectomy. It was not possible to confidently describe the actual method used from the information available from the trials. For analysis purposes these techniques have therefore been considered together.

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 12*. Thirteen RCTs, reported in 17 papers,[123,130,131,136,139,145,149,151,154,163,177–179,234–237] were eligible for this comparison, in which a total of 1231 participants were randomised. The total number allocated to laser coagulation was 612 and the total number allocated to TURP was 619.

Five studies took place in the UK,[136,139,145,154,179] three in the US,[130,163,177] and one each in Sweden,[131] Australia,[123] Spain,[149] Korea[151] and the Netherlands.[178] Six studies provided details on recruitment dates.[130,131,145,151,163,178] The earliest recruitment date was August 1991[163] and the latest recruitment date was December 2002.[151]

Overall, the total numbers of participants with moderate and severe symptoms allocated to receive laser coagulation were 353 (61%) and 225 (39%) respectively. There were 343 (58%) moderately and 239 (41%) severely symptomatic participants allocated to TURP.

In general, studies reported prostate size. Two studies[154,179] failed to report prostate size of the enrolled participants and in one study[149] authors reported that, to be included, patients had to have prostate sizes between 20 and 60 g. The total numbers of participants who had small, moderate-sized and large prostates in the laser coagulation group were 23 (5%), 34 (8%) and 387 (87%) respectively. Of those allocated to a TURP procedure, 22 (5%) had a small prostate, 176 (39%) had a moderate-sized prostate and 214 (48%) had a large prostate.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.4. The results of the meta-analyses are given in Appendix 9.4. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

Of the 13 eligible RCTs, six provided information on the mean or median IPSS/AUA scores 3 months after surgery.[131,149,151,177–179] Two studies[149,177] showed better scores in the laser group than in the TURP group, and four[131,151,178,179] favoured TURP. This variation may be explained by the fact that trials included participants with various levels of prostate size. For example, in the trial by Kabalin and colleagues,[177] participants had an average prostate size of 17 g (ml) in the TURP group, whereas in the study reported by Mårtenson and colleagues,[178] participants randomised to TURP had on average a prostate size of 50 ml (g). Because of this heterogeneity we opted not to derive a pooled estimate (*Figure 12*, comparison 04:01:01).

At 12 months

IPSS/AUA scores were reported in a total of seven studies.[131,145,151,163,177–179] The direction and size of effect varied across the studies. The improvements in IPSS reported by Cowles and colleagues[163] and Liedberg and colleagues[131] were, however, consistently lower in the laser coagulation intervention group (*Figure 12*, comparison 04:01:03).

TABLE 12 *Summary of the baseline characteristics, laser coagulation vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Chacko *et al.*, 2001;[154] CLasP study	Laser coagulation	74	74	17.6	NR	NR	NR
	TURP	74	73	19.4	NR	NR	NR
Costello *et al.*, 1995[123]	Laser coagulation	34	68	NR	8.76	NR	30
	TURP	37	68	NR	9.48	NR	34
Cowles *et al.*, 1995[163]	Laser coagulation	56	65	18.7	8.9	163	42
	TURP	59	67	20.8	9.5	207	39
Donovan *et al.*, 2000;[136] CLasP study	Laser coagulation	117	67	19.1	10.4	124	41
	TURP	117	66	19.2	10.3	104	38
Gujral *et al.*, 2000;[139] CLasP study	Laser coagulation	38	70	20.9	11.2	438	41[c]
	TURP	44	70	19.5	8.5	545	50[c]
Kabalin *et al.*, 1995[177]	Laser coagulation	13	65	20.9	8.5	236	24[b]
	TURP	12	69	18.8	9.0	291	17[b]
Kim *et al.*, 2006[151]	Laser coagulation	89	69	21.1	8.6	219	43
	TURP	110	67	24.0	11.9	187	44
Kursh *et al.*, 2003[130]	Laser coagulation	37	68	24.0[c]	9.2[c]	81[c]	41[c]
	TURP	35	69	23.0[c]	9.1[c]	87[c]	40[c]
Liedberg *et al.*, 2003[131]	Laser coagulation	20	NR	19[c]	8[c]	96[c]	49[c]
	TURP	11	NR	17[c]	8[c]	117[c]	47[c]
Mårtenson and de la Rosette, 1999[178]	Laser coagulation	30	> 45	21.7	7.3	116	46
	TURP	14	> 45	21.6	9.3	88	50
McAllister *et al.*, 2000[145]	Laser coagulation	76	68	18.1	9.6	113	NR
	TURP	75	68	18.2	10.0	120.7	NR
Rodrigo Aliaga *et al.*, 1998[149]	Laser coagulation	18	NR	25.5	7.0	77	20–60[b]
	TURP	21	NR	24.2	8.3	89	20–60[b]
Suvakovic and Hindmarsh, 1996[179]	Laser coagulation	10	67	15.7	10.5	47	24[b]
	TURP	10	66	18.8	11.1	162	22[b]

NR, not reported.; TURP, transurethral resection of the prostate.
Data given as mean values (unless stated otherwise).
a Symptom scores given as IPSS/AUA.
b Grams.
c Median.

Longer-term follow-up

Symptom scores data at 2 years were reported in three studies.[130,177,178] Again, there was considerable variation between the trials (*Figure 12*, comparison 04:01:05).

Complications

Complications listed by study are detailed in Appendix 8.4, *Table 58*. Seventeen types of complications were reported to varying extents across the 13 studies. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 13*). Results for other complications are presented in Appendix 9.4, comparison 04:02. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied. For urinary incontinence it was unclear whether the type of incontinence considered was the same across all studies.

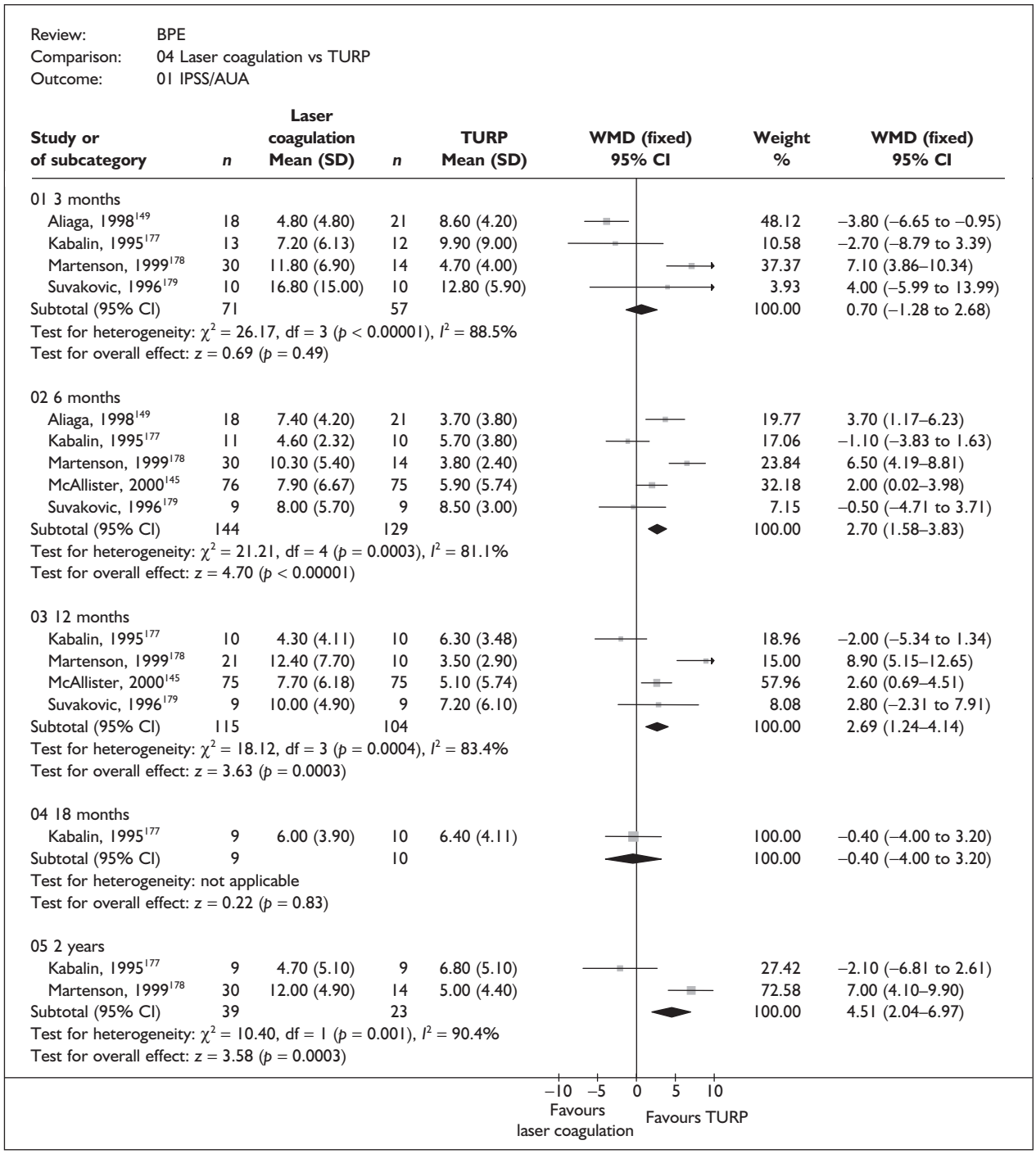


FIGURE 12 *Symptom scores, laser coagulation vs TURP.*

Review: BPE
Comparison: 04 Laser coagulation vs TURP
Outcome: 02 Complications

Study or subcategory	Laser coagulation n/N	TURP n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 Blood transfusion					
Aliaga, 1998[149]	0/18	1/21		2.88	0.39 (0.02–8.93)
Chacko, 2001[154]	0/74	4/74		9.31	0.11 (0.01–2.03)
Costello, 1995[123]	0/34	3/37		6.94	0.16 (0.01–2.90)
Cowles, 1995[163]	0/56	2/59		5.04	0.21 (0.01–4.29)
Donovan, 2000[136]	1/117	1/117		2.07	1.00 (0.06–15.80)
Gujral, 2000[139]	0/38	3/44		6.72	0.16 (0.01–3.09)
Kabalin, 1995[177]	0/13	1/12		3.22	0.31 (0.01–6.94)
Kim, 2006a[151]	0/89	19/101		37.81	0.03 (0.00–0.47)
Kursh, 2003[130]	0/35	0/35			Not estimable
Martenson, 1999[178]	0/30	0/14			Not estimable
McAllister, 2000[145]	0/76	12/75		26.02	0.04 (0.00–0.66)
Subtotal (95% CI)	580	589		100.00	0.11 (0.04–0.26)
Total events: 1 (Laser coagulation), 46 (TURP)					
Test for heterogeneity: $\chi^2 = 5.30$, df = 8 ($p = 0.72$), $I^2 = 0\%$					
Test for overall effect: $z = 4.81$ ($p < 0.00001$)					
02 Urinary retention					
Cowles, 1995[163]	17/56	5/59		53.41	3.58 (1.42–9.06)
Kim, 2006a[151]	2/89	4/101		41.10	0.57 (0.11–3.02)
Suvakovic, 1996[179]	1/10	0/10		5.48	3.00 (0.14–65.90)
Subtotal (95% CI)	155	170		100.00	2.31 (1.11–4.80)
Total events: 20 (Laser coagulation), 9 (TURP)					
Test for heterogeneity: $\chi^2 = 3.59$, df = 2 ($p = 0.17$), $I^2 = 44.3\%$					
Test for overall effect: $z = 2.25$ ($p = 0.02$)					
03 Urinary tract infection					
Costello, 1995[123]	1/34	4/37		12.35	0.27 (0.03–2.32)
Donovan, 2000[136]	3/117	2/117		6.45	1.50 (0.26–8.81)
Gujral, 2000[139]	1/38	2/44		5.97	0.58 (0.05–6.14)
Kim, 2006a[151]	7/89	7/101		21.14	1.13 (0.41–3.11)
Kursh, 2003[130]	7/35	4/35		12.89	1.75 (0.56–5.45)
Liedberg, 2003[131]	16/20	1/11		4.16	8.80 (1.34–57.76)
Martenson, 1999[178]	10/30	4/14		17.58	1.17 (0.44–3.08)
McAllister, 2000[145]	20/76	6/75		19.47	3.29 (1.40–7.73)
Subtotal (95% CI)	439	434		100.00	1.84 (1.22–2.79)
Total events: 65 (Laser coagulation), 30 (TURP)					
Test for heterogeneity: $\chi^2 = 10.21$, df = 7 ($p = 0.18$), $I^2 = 31.4\%$					
Test for overall effect: $z = 2.88$ ($p = 0.004$)					
04 Stricture					
Costello, 1995[123]	2/34	2/37		9.69	1.09 (0.16–7.30)
Cowles, 1995[163]	0/56	9/59		46.85	0.06 (0.00–0.93)
Kabalin, 1995[177]	0/13	1/12		7.87	0.31 (0.01–6.94)
Kim, 2006a[151]	0/89	7/101		35.59	0.08 (0.00–1.30)
Liedberg, 2003[131]	0/20	0/11			Not estimable
Subtotal (95% CI)	212	220		100.00	0.18 (0.06–0.56)
Total events: 2 (Laser coagulation), 19 (TURP)					
Test for heterogeneity: $\chi^2 = 4.54$, df = 3 ($p = 0.21$), $I^2 = 33.9\%$					
Test for overall effect: $z = 2.97$ ($p = 0.003$)					
05 TUR syndrome					
Chacko, 2001[154]	0/74	2/74		38.51	0.20 (0.01–4.10)
Cowles, 1995[163]	0/56	2/59		37.52	0.21 (0.01–4.29)
Kabalin, 1995[177]	0/13	1/12		23.96	0.31 (0.01–6.94)
Subtotal (95% CI)	143	145		100.00	0.23 (0.04–1.34)
Total events: 0 (Laser coagulation), 5 (TURP)					
Test for heterogeneity: $\chi^2 = 0.05$, df = 2 ($p = 0.98$), $I^2 = 0\%$					
Test for overall effect: $z = 1.64$ ($p = 0.10$)					
06 Urinary incontinence					
Chacko, 2001[154]	0/74	3/74		27.66	0.14 (0.01–2.72)
Cowles, 1995[163]	0/56	2/59		19.25	0.21 (0.01–4.29)
Kim, 2006a[151]	0/89	4/101		33.34	0.13 (0.01–2.31)
Kursh, 2003[130]	0/35	2/35		19.76	0.20 (0.01–4.02)
Martenson, 1999[178]	0/30	0/14			Not estimable
Subtotal (95% CI)	284	283		100.00	0.16 (0.04–0.71)
Total events: 0 (Laser coagulation), 11 (TURP)					
Test for heterogeneity: $\chi^2 = 0.08$, df = 3 ($p = 0.99$), $I^2 = 0\%$					
Test for overall effect: $z = 2.41$ ($p = 0.02$)					

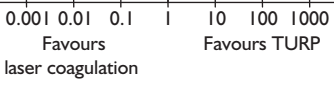


FIGURE 13 *Complications, laser coagulation vs TURP.*

Blood transfusion

One (0.2%) laser patient as opposed to 46 (7.8%) TURP patients required a blood transfusion (*Figure 13*, comparison 04:02:01: RR 0.11, 95% CI 0.04–0.26, $p < 0.001$).[123,130,136,139,145,149,151,154,163,177,178]

Urinary retention

The pooling of data from three studies[151,163,179] showed that 13% ($n = 20$) of the patients following laser coagulation had urinary retention compared with 5% ($n = 9$) of those following TURP (*Figure 13*, comparison 04:02:02: RR 2.31, 95% CI 1.11–4.80, $p = 0.02$).

Urinary tract infection

Meta-analysis of eight trials[123,130,131,136,139,145,151,178] suggested that the incidence of urinary tract infection was higher following laser coagulation than after TURP (*Figure 13*, comparison 04:02:03: 65/439 versus 30/434, RR 1.84, 95% CI 1.22–2.79, $p = 0.004$). Note that three trials had particularly high rates of infection and that two and three of the infections in the laser and TURP groups, respectively, were actually epididymitis. These results should also be treated with caution as the length of follow-up of the RCTs varied.

Stricture

In five RCTs with data,[123,131,151,163,177] a total of two (0.9%) strictures were reported amongst 212 participants allocated to laser procedures versus 19 (8.6%) strictures amongst 220 participants allocated to TURP procedures (*Figure 13*, comparison 04:02:04: RR 0.18, 95% CI 0.06–0.56, $p = 0.003$).

TUR syndrome

Based on data from three trials[154,163,177] the incidence of TUR syndrome after laser coagulation and TURP was 0% (0/143) and 3.4% (5/145) respectively; however, this difference was not statistically significant (*Figure 13*, comparison 04:02:05: RR 0.23, 95% CI 0.04–1.34, $p = 0.10$).

Incontinence

A total of five studies[130,151,154,163,178] reported urinary incontinence. The rates of incontinence were consistently lower following laser coagulation than following TURP (*Figure 13*, comparison 04:02:06: 0/284 versus 11/283; RR 0.16, 95% CI 0.04–0.71, $p = 0.02$).

Quality of life

Six studies,[130,136,139,151,154,178] using a variety of instruments, reported the quality of life of people following laser coagulation or TURP (Appendix 8.4, *Table 59*). In four studies[136,139,151,154] the quality of life was assessed using the IPSS QoL (0–6) questionnaire. In one study[130] the AUA quality of life questionnaire was used and another study[178] used the quality of life index.

In three studies providing data,[130,151,178] the quality of life scores were poorer following laser coagulation than following TURP at 3, 12 and 24 months (*Figure 14*, comparison 04:10). Meta-analysis of the change of quality of life from baseline reported in three trials[136,139,154] was consistent with this although the difference between the groups was not statistically significant (*Figure 14*, comparison 04:11).

Urodynamic outcomes

Data on peak urine flow rate, total voided volume, residual volume, detrusor pressure and prostate size were reported across ten studies.[130,131,139,145,149,151,163,177–179] These are tabulated in Appendix 8.4, *Table 60*. Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 9.4, comparisons 04:04–04:08.

At 3 months

All eight studies that provided information on peak urine flow rates at 3 months after operation reported lower mean or median flow rates in the laser coagulation group (Appendix 8.4, *Table 60*). Meta-analysis of five RCTs[145,149,177–179] reporting data suitable for quantitative synthesis gave a WMD of –5.36 ml/s (95% CI –7.28 to –3.45, $p < 0.001$) favouring TURP. This result should be treated with caution as two studies failed to report how many patients contributed to the analysis.

At 12 months

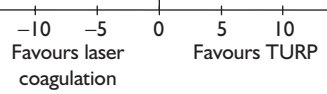
A total of six studies[131,145,163,177–179] provided details on peak urine flow rate at 12 months after operation. All but one study[177] reported higher median or mean peak urine flow rates in the TURP group. In the four studies[145,177–179] that presented means and standard deviations, the WMD was –4.57 ml/s (Appendix 9.4, comparison 04:04:03: 95% CI –6.55 to –2.59, $p < 0.001$). There was evidence of statistical heterogeneity amongst the studies included in the meta-analysis. Using a random-effects model did not change this result. Cowles and colleagues[163] reported change from baseline rather than absolute rates. Their results were consistent with those of the meta-analysis.

Longer-term follow-up

Two studies[177,178] reported peak urine flow rates at 2 years after laser coagulation and TURP. Meta-

Review: BPE
Comparison: 04 Laser coagulation vs TURP
Outcome: 10 Quality of Life

Study or subcategory	*n*	Laser coagulation Mean (SD)	*n*	TURP Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Martenson, 1999[178]	30	2.30 (1.40)	14	0.90 (1.30)		100.00	1.40 (0.55–2.25)
Subtotal (95% CI)	30		14			100.00	1.40 (0.55–2.25)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 3.25$ ($p = 0.001$)							
02 6 months							
Martenson, 1999[178]	30	2.20 (1.40)	14	0.50 (0.70)		100.00	1.70 (1.08–2.32)
Subtotal (95% CI)	30		14			100.00	1.70 (1.08–2.32)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 5.37$ ($p < 0.00001$)							
03 12 months							
Martenson, 1999[178]	30	2.20 (1.50)	14	0.60 (0.80)		100.00	1.60 (0.92–2.28)
Subtotal (95% CI)	30		14			100.00	1.60 (0.92–2.28)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 4.61$ ($p < 0.00001$)							
04 2 years							
Martenson, 1999[178]	30	2.20 (1.50)	14	0.70 (0.90)		100.00	1.50 (0.79–2.21)
Subtotal (95% CI)	30		14			100.00	1.50 (0.79–2.21)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 4.12$ ($p < 0.0001$)							



Review: BPE
Comparison: 04 Laser coagulation vs TURP
Outcome: 11 Change in quality of life

Study or subcategory	*N*	Laser coagulation Mean (SD)	*N*	TURP Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 7.5 months							
Chacko, 2001[154]	49	−3.10 (1.96)	45	−3.42 (1.59)		26.83	0.32 (−0.40 to 1.04)
Donovan, 2000[136]	93	−1.90 (1.72)	85	−2.20 (1.65)		56.56	0.30 (−0.20 to 0.80)
Gujral, 2000[139]	30	−2.80 (1.80)	33	−3.20 (1.90)		16.61	0.40 (−0.51 to 1.31)
Subtotal (95% CI)	172		163			100.00	0.32 (−0.05 to 0.69)
Test for heterogeneity: $\chi^2 = 0.04$, df = 2 ($p = 0.98$), $I^2 = 0\%$							
Test for overall effect: $z = 1.69$ ($p = 0.09$)							

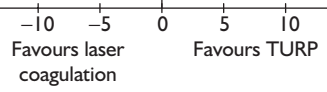


FIGURE 14 *Quality of life, laser coagulation vs TURP*

analysis of data from these studies did not show any statistically significant difference in peak urine flow rate between the two arms (Appendix 9.4, comparison 04:04:06: WMD –0.76, 95% CI –5.30 to 3.77, $p = 0.74$). Note that the number of patients available for this follow-up assessment is unclear.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.4, *Table 61*. Information on duration of operation, length of hospital stay and reoperations was identified to a varying extent across the 13 eligible studies.

Duration of operation

Duration of operation was reported in five trials.[123,151,163,177,179] Combining data from two trials[163,179] indicated that the duration of operation in the laser coagulation arm was statistically significantly shorter than that for the TURP arm (Appendix 9.4, comparison 04:12: WMD –12.24 minutes, 95% CI –16.78 to –7.69, $p < 0.001$). This result is consistent with findings from trials whose data were not amenable to meta-analysis. There was evidence of statistical heterogeneity. Using a random-effects model resulted in the difference no longer being significant (WMD –11.54, 95% CI –31.74 to 8.65, $p = 0.29$). The sources of heterogeneity were unclear. However, patients included in the trial by Suvakovic and Hindmarsh[179] had considerably smaller prostates than those included in the trial by Cowles and colleagues.[163] In addition, there was a high degree of uncertainty surrounding the results from the former trial because of the small sample size.

TABLE 13 *Summary of the clinical effect sizes from meta-analyses, laser coagulation vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	4 (6)	0.70[a]	–1.28 to 2.68	0.49
12 months	4 (7)	2.69[a]	1.24–4.14	< 0.001
Longer term	2 (3)	4.51[a]	2.04–6.97	< 0.001
Blood transfusion	10 (10)	0.11[b]	0.04–0.26	< 0.001
Urinary retention	3 (3)	2.31[b]	1.11–4.80	0.02
Urinary tract infection	8 (8)	1.84[b]	1.22–2.79	0.004
Stricture	5 (5)	0.18[b]	0.06–0.56	0.003
TUR syndrome	3 (3)	0.23[b]	0.04–1.34	0.10
Incontinence	5 (5)	0.16[b]	0.04–0.71	0.02
Quality of life				
3 months	1 (2)	1.40[a]	0.55–2.25	0.001
12 months	1 (3)	1.60[a]	0.92–2.28	< 0.001
Longer term	1 (3)	1.50[a]	0.79–2.21	< 0.001
Q_{max}				
3 months	5 (8)	–5.36[a]	–7.28 to –3.45	< 0.001
12 months	4 (7)	–4.57[a]	–6.55 to –2.59	< 0.001
Longer term	2 (3)	–0.76[a]	–5.30 to 3.77	0.74
Duration of operation	2 (5)	–12.24[a]	–16.78 to –7.69	< 0.001
Length of hospital stay	2 (10)	–1.33[a]	–1.68 to –0.98	< 0.001
Reoperation	9 (9)	3.21[b]	1.63–6.32	0.0008

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

Length of hospital stay

Nine out of ten studies providing information on length of hospital stay reported lower mean or median stay in the laser coagulation group. Two RCTs reported data suitable for quantitative synthesis.[145,163] Across them, the average length of stay was significantly shorter in the laser coagulation group than in the TURP group (Appendix 9.4, comparison 04:13: WMD –1.33; 95% CI –1.68 to –0.98, $p < 0.001$).

Reoperation

A total of nine RCTs[123,130,139,145,151,154,163,177,178] provided information on reoperation rates. The results of the meta-analysis showed a statistically significant higher rate following laser coagulation (Appendix 9.4, comparison 04:02:16: RR 3.21, 95% CI 1.65–6.24, $p < 0.001$). As the length of follow-up ranged from 6 months[123] to 5 years,[145] the results of this meta-analysis should be treated with caution.

Summary and conclusions of the evidence for and against the intervention

Data from over 1000 participants randomised across 13 RCTs of generally moderate to poor quality (or reporting) were included. The data indicate that symptom scores at 12 months or more and quality of life and peak urine flow rate at 3 and 12 months are worse after laser coagulation than after TURP. The occurrence of blood transfusion, strictures and urinary incontinence was lower in the laser coagulation group but urinary retention and urinary tract infection appeared to be higher. TUR syndrome does not appear to differ between the two approaches. In terms of descriptors of care, the data suggest that duration of operation and length of hospital stay are likely to be shorter after laser coagulation than after TURP but that the reoperation rate is higher after laser coagulation than after TURP.

The results for symptom scores, peak urine flow rate and duration of operation displayed significant heterogeneity. There was consistency in the direction and size of effect across the studies for all except symptom scores. This heterogeneity may be due to variations in the characteristics of the randomised participants, particularly differences in baseline prostate size and symptom score. It may also be due to differences in the specific aims and objectives of the trials, which led to important differences in inclusion criteria.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 13*.

Chapter 7

Clinical effectiveness of transurethral incision of the prostate

Transurethral incision of the prostate (TUIP) versus TURP

Characteristics of included studies

The baseline characteristics of the included studies are summarised in *Table 14*. A total of 871 participants were randomised across 11 eligible RCTs and reported in 14 papers.[135,149,152,157,180–186,238–240] The total number of people allocated to TUIP was 430 and the total allocated to TURP was 441.

Two studies took place in the US,[135,152] two in Denmark,[180,183] and one each in Spain,[149] Finland,[157] Sweden,[181] Hong Kong,[182] India,[185] Israel[184] and Poland.[186] Three studies provided details on recruitment dates,[135,152,181] with the earliest recruitment being January 1985[152] and the latest August 1990.

In terms of symptom scores, two studies reported IPSS/AUA scores[149,186] and four reported Madsen–Iversen scores.[135,152,180,181] Of the studies reporting IPSS/AUA scores, 50 participants allocated to TUIP had moderate symptoms of BPE and 20 had severe symptoms compared with 21 with severe and 50 with moderate symptoms among those allocated to TURP.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.5. The results of the meta-analyses are given in Appendix 9.5. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

Of the 11 eligible RCTs, five reported IPSS/AUA or Madsen scores at 3 months, although for only one of these the data were reported in a way that was potentially amenable to analysis and there was no evidence of a statistically significant difference. Two tended to favour TUIP, one TURP and two showed no difference.

At 12 months

Data describing IPSS/AUA scores at 12 months were available for six trials but, again, only one provided means and standard deviations. Again, no clear pattern emerged: three tended to favour TURP, one TUIP and two showed no difference.

Longer-term follow-up

Losses to follow-up were high in nearly all studies reporting long-term follow-up. Only one study[181] reported Madsen scores at 5 years following operation. No significant differences were observed between the TUIP and TURP groups (Appendix 8.5, *Table 62*). Data for other follow-up times (2 and 3 years) were also reported by Christensen and colleagues,[135] Jahnson and colleagues,[181] Riehmann and colleagues[152] and Saporta and colleagues.[184] These can be seen in Appendix 8.5 and the respective forest plots in Appendix 9.5, comparison 05:02.

Complications

Data describing 18 types of complications are tabulated in Appendix 8.5, *Table 63*. Although some data were estimated from the reports of ten trials, data describing individual complications were available from more than half of the 11 trials for only five of the 18 complications. The reliability and usefulness of data for the other 13 were therefore very limited. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 15*). Results for other complications are presented in Appendix 9.5, comparison 05:03. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied. For urinary incontinence it was unclear if the type of incontinence considered was the same across all studies.

Blood transfusion

Seven studies[149,157,180–183,185] provided information on blood transfusions. There were fewer blood transfusions following TUIP in all except one trial, which reported no transfusions in either group

TABLE 14 *Summary of the baseline characteristics, TUIP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Rodrigo Aliaga *et al.*, 1998[149]	TUIP	20	NR	24.2	8.7	89	20–60[b]
	TURP	21	NR	24.4	8.3	146	20–60[b]
Christensen *et al.*, 1990[135]	TUIP	38	63[c]	16[d]	7.8	NR	≤20
	TURP	38	62[c]	16[d]	9.7	NR	≤20
Dørflinger *et al.*, 1992[180]	TUIP	29	69	15[d]	10	NR	≤20
	TURP	31	71	15[d]	8	NR	≤20
Hellström *et al.*, 1986[157]	TUIP	11	63	NR	8.6	62	≤30
	TURP	13	59	NR	7.5	43	≤30
Jahnson *et al.*, 1998[181]	TUIP	42	71	15.8[d]	8.5	109	20–40
	TURP	43	70	15.4[d]	9.0	139	20–40
Li and Ng, 1987[182]	TUIP	29	65	NR	NR	NR	≤30
	TURP	30	70	NR	NR	NR	≤30
Nielsen, 1988[183]	TUIP	25	73[c]	NR	5[c]	NR	NR
	TUIP	24	69[c]	NR	5[c]	NR	NR
Riehmann *et al.*, 1995[152]	TUIP	56	64	15.0[d]	11	NR	NR
	TURP	61	65	15.5[d]	9	NR	NR
Saporta *et al.*, 1996[184]	TUIP	20	66.8	NR	NR	NR	≥40
	TURP	20	71.4	NR	NR	NR	≥40
Soonawalla and Pardanani, 1992[185]	TUIP	110	65.0	NR	NR	NR	NR
	TURP	110	62.2	NR	NR	NR	NR
Tkocz and Prajsner, 2002[186]	TUIP	50	63	17.1	7.6	75	27.0
	TURP	50	63	17.1	6.9	68	28.2

NR, not reported; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.
Data given as mean values (unless otherwise stated).
a Symptom scores given as IPSS/AUA (unless stated otherwise).
b Grams
c Median.
d Madsen score.

(*Figure 15*, comparison 05:03:01: 3/266 (11%) versus 77/272 (28%), RR 0.06, 95% CI 0.03–0.16, $p < 0.001$), reflecting particularly high rates of transfusion following TURP in four trials.

Urinary retention

Meta-analysis of data from four trials[181–183,185] reporting urinary retention showed no statistically significant difference between the TUIP and TURP groups and wide confidence intervals (*Figure 15*, comparison 05:03:02: 10/206 versus 5/207, RR 1.84, 95% CI 0.70–4.86, $p = 0.22$). The direction of effect varied across studies with one trial favouring TUIP,[181] two favouring TURP[183,185] and one showing no difference.[182]

Urinary tract infection

Only one study reported the incidence of urinary tract infections (including epididymo-orchitis) following surgery.[185] A total of five (4.5%) infections were reported amongst 110 participants allocated to TUIP compared with two (1.8%) infections

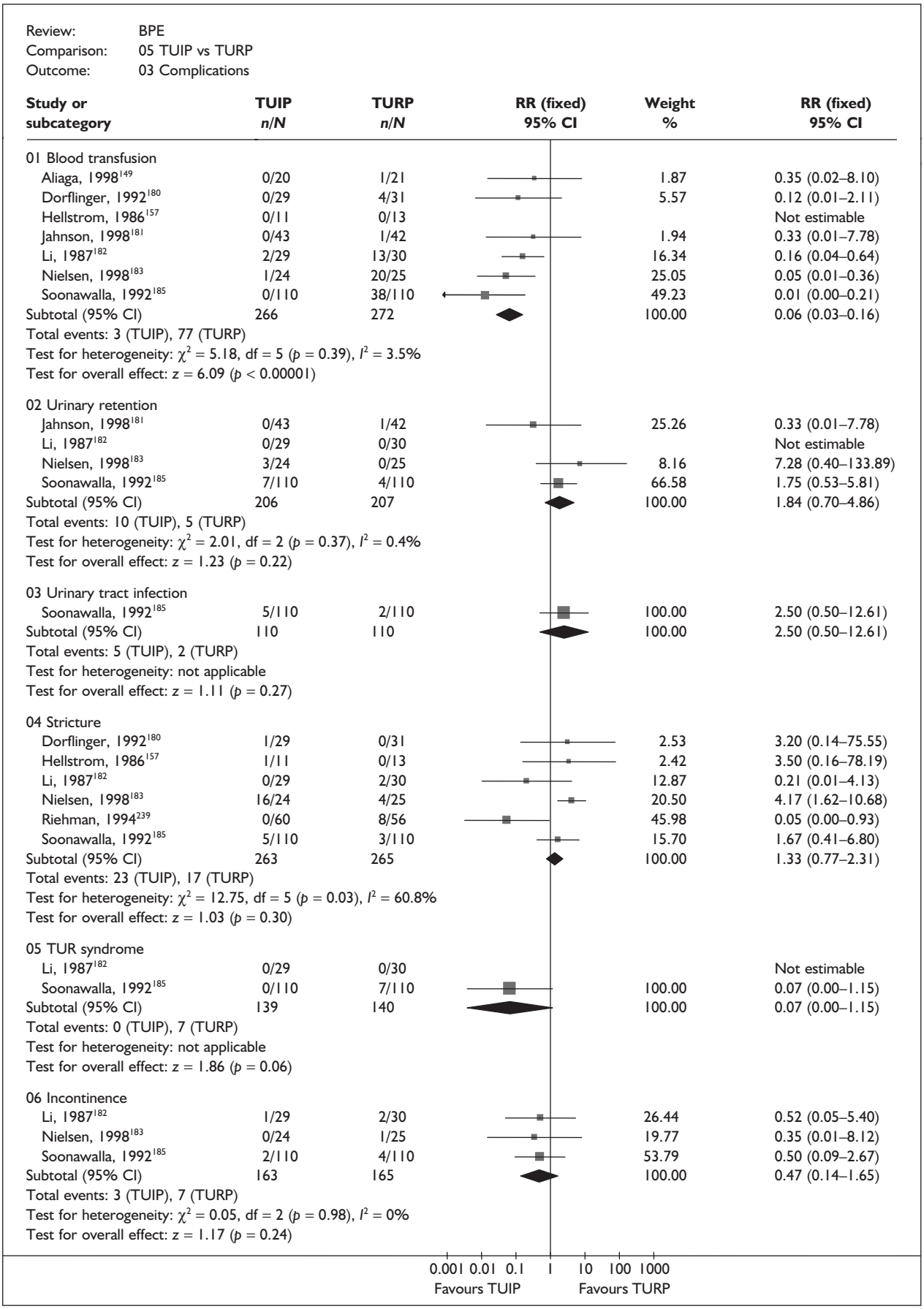


FIGURE 15 *Complications, TUIP vs TURP.*

amongst 110 allocated to TURP (*Figure 15*, comparison 05:03:03: RR 2.50, 95% CI 0.50–12.61, $p = 0.27$).

Stricture

Six studies provided data on strictures.[152,157,180,182,183,185] There was marked heterogeneity across the studies, with no clear pattern of results (*Figure 15*, comparison 05:03:04: 23/263 versus 17/265, RR 1.33, 95% CI 0.77–2.31, $p = 0.30$). The source of heterogeneity was uncertain, although the lack of separation between urethral stricture and bladder neck contracture may have been a factor as definitions of these conditions varied across the trials. In addition, the length of follow-up varied across studies.

TUR syndrome

TUR syndrome was reported in two studies.[182,185] No cases of a TUR syndrome were recorded in patients randomised to the TUIP arm. On the other hand, 6.4% of the patients (all in one trial) allocated to TURP had TUR syndrome (*Figure 15*, comparison 05:03:05: 0/139 versus 7/140, RR 0.07, 95% CI 0.00–1.15, $p = 0.06$).

Urinary incontinence

Meta-analysis of three trials that reported urinary incontinence showed no statistically significant difference between the TUIP and the TURP groups even though there were fewer events in the TUIP group (*Figure 15*, comparison 05:03:06: 3/163 versus 7/165, RR 0.47, 95% CI 0.14–1.65, $p = 0.24$). This result should be interpreted with caution as the length of follow-up varied, the types of incontinence were not fully described across studies and the confidence interval is wide.

Quality of life

Only one study[186] reported quality of life of patients following surgery using the IPSS QoL (0–6) questionnaire. At 2 years, quality of life appeared to be marginally higher for those patients who underwent TURP (Appendix 9.5, comparison 05:08:01: WMD 0.20, 95% CI 0.01–0.39, $p = 0.04$).

Urodynamic outcomes

Data on peak urine flow rate, mean urine flow rate, total voided volume, residual volume and detrusor pressure were reported to a varying extent across eleven studies.[135,149,152,157,180–186] These are tabulated in Appendix 8.5, *Table 65*. Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 9.5, comparisons 05:05–05:07.

At 3 months

Nine studies[135,149,152,157,180–183,185] provided peak urine flow rate measurements at 3 months for patients treated with TUIP and TURP (Appendix 8.5, *Table 65*). Seven studies[135,152,157,180,181,183,185] showed that patients in the TURP group achieved a higher mean or median peak urine flow rate than patients in the TUIP group, and two studies[149,182] showed a higher value in the TUIP group. Only three RCTs[149,157,182] presented data that were sufficiently similar to allow quantitative synthesis (Appendix 9.5, comparison 05:05:01). Meta-analysis showed no statistically significant difference between the groups (WMD –0.07 ml/s, 95% CI –3.53 to 3.39, $p = 0.97$).

At 12 months

All six studies[135,180,181,183–185] that provided information on the mean or median peak urine flow rate for patients 12 months after surgery reported lower mean or median peak urine flow rates following TUIP (Appendix 8.5, *Table 65*). Only one study[184] reported data that were suitable for analysis (Appendix 9.5, comparison 05:05:03: MD –2.71 ml/s, 95% CI –5.77 to 0.35, $p = 0.08$).

Longer-term follow-up

Two studies[152,181] provided 5-year results. A total of 26 and 32 patients were available for analysis in the TUIP and TURP groups respectively. In both studies the mean peak flow rate was lower for TUIP than it was for TURP.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.5, *Table 66*. Information on duration of operation, length of hospital stay and reoperation rates was identified to a varying extent across the 11 eligible studies for this comparison.

Duration of operation

Seven studies[152,157,180–183,185] provided information on the duration of operation (Appendix 8.5, *Table 66*). In all studies the duration of operation was shorter in the TUIP group. Only two studies[157,182] presented data in a sufficiently similar form to allow quantitative synthesis (Appendix 9.5, comparison 05:09]; a TUIP procedure was 18.9 minutes shorter than TURP (95% CI –24.13 to –13.67, $p < 0.001$). This result was consistent with the other five studies reporting medians.

Length of hospital stay

Eight studies[135,149,152,157,180,182,183,185] provided information on length of hospital stay (Appendix

8.5, *Table 66*). Despite marked differences between studies in overall length of stay, in six[135,149,152,157,182,185] they reported it to be shorter for TUIP and in two [180,183] there was no difference. Two RCTs[157,182] reported data that were suitable for synthesis. Across them, the average length of stay was significantly shorter in the TUIP group than in the TURP group (Appendix 9.5, comparison 05:10: WMD –2.26 days, 95% CI –3.81 to –0.71, $p = 0.004$). The within-trial differences in medians tended to be smaller than this.

Reoperation

Reoperations were reported in seven trials.[135,149,152,180,181,183,184] Reoperation was more common in the TUIP groups (17.5%) than in the TURP groups (9%) (Appendix 9.5, comparison 05:04:18: RR 1.87, 95% CI 1.16–3.03, $p = 0.01$). It should be noted that differences between studies in timing and completeness of follow-up might have introduced bias.

Summary and conclusions of the evidence for and against the intervention

This review considered data from 871 randomised participants across 11 RCTs of moderate to poor quality (and reporting). There is no evidence that the two interventions are different in terms of symptomatic outcome as no clear pattern emerged. The data indicate that, after TUIP, improvements in peak urine flow rate and quality of life are lower than after TURP, whereas the rate of blood transfusion and occurrence of TUR syndrome are higher after TURP than after TUIP. Urinary retention, urinary tract infection, strictures and incontinence do not appear to differ between the two approaches, although clinically important differences could not be ruled out. TUIP appears to be associated with shorter duration of operation and length of hospital stay but the reoperation rate is higher. It is important to note that the latest recruitment date was August 1990 and so the TURP outcomes then and now would not be comparable given the improvements in TURP technology over the past 16 years, reflected best by the higher transfusion rates reported in the seven trials included in this review of TUIP versus TURP.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 15*. These should be interpreted in view of the comments mentioned earlier in this chapter.

TABLE 15 *Summary of the clinical effect sizes from meta-analyses, TUIP vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	1 (1)	–0.50[a]	–3.35 to 2.35	0.73
12 months	1 (1)	–1.00[a]	–1.73 to –0.27	0.007
Longer term	NR	NR	NR	NR
Madsen–Iversen score				
3 months	0 (3)	NR	NR	NR
12 months	1 (5)	0.34[a]	–1.55 to 2.23	0.72
Longer term	1 (3)	1.21[a]	–0.87 to 3.29	0.26
Blood transfusion	7 (7)	0.06[b]	0.03–0.16	< 0.001
Urinary retention	4 (4)	1.84[b]	0.70–4.86	0.22
Urinary tract infection	1 (1)	2.50[b]	0.50–12.61	0.27
Stricture	6 (6)	1.33[b]	0.77–2.31	0.30
TUR syndrome	2 (2)	0.07[b]	0.00–1.15	0.06
Incontinence	4 (4)	0.47[b]	0.14–1.65	0.24
Quality of life				
3 months	NR	NR	NR	NR
12 months	NR	NR	NR	NR
Longer term	1	0.20[a]	0.01–0.39	0.04
Q_{max}				
3 months	3 (9)	–0.07[a]	–3.53 to 3.39	0.97
12 months	1 (6)	–2.71[a]	–5.77 to 0.35	0.08
Longer term	1 (2)	–1.71[a]	–4.74 to 1.32	0.27
Duration of operation	2 (7)	–18.90[a]	–24.13 to –13.67	< 0.001
Length of hospital stay	2 (8)	–2.26[a]	–3.81 to –0.71	0.004
Reoperation	7 (7)	1.87[b]	1.16–3.03	0.01

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; NR, not reported; TUIP, transurethral incision of the prostate; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

Chapter 8

Clinical effectiveness of other ablative techniques

Interventions using laser technology

Holmium laser resection versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 16*. Five RCTs, reported in 15 papers,[63,64,69,134,187–189,241–248] were eligible for this comparison, in which a total of 580 participants were randomised.

Two trials took place in New Zealand[134,189] and one trial each in India,[187] Italy[188] and Egypt.[64] Recruitment dates were reported in all five studies and ranged from April 1996 to December 2003.

All five studies provided details of the participants' IPSS/AUA symptom scores and prostate size, showing that all 580 participants had severe symptoms and large prostates at trial entry.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.6 and also in *Figure 16*. The results of the meta-analyses are given in Appendix 9.6. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

Out of the five eligible studies for this comparison, only two reported IPSS/AUA symptom scores at 3 months after surgery.[189,248] No statistically significant differences were observed between the two groups (*Figure 16*, comparison 06:01:01: WMD –0.47, 95% CI –1.92 to 0.98, $p = 0.53$).

At 12 months

Five trials reported IPSS/AUA scores measured within 12 months. Pooling of the data displayed statistically significantly lower scores for laser resection (*Figure 16*, comparison 06:01:03)

TABLE 16 *Summary of the baseline characteristics, laser resection vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Gupta *et al.*, 2006[187]	Laser resection	50	66	23.4	5.1	112	58
	TURP	50	66	23.3	4.5	84	60
Kuntz *et al.*, 2004[64]	Laser resection	100	68	22.1	4.9	238	53
	TURP	100	69	21.4	5.9	216	50
Montorsi *et al.*, 2004[188]	Laser resection	52	65	21.6	8.2	4	70
	TURP	48	64	21.9	7.8	4	56
Westenberg *et al.*, 2004[189]	Laser resection	61	67	21.9	8.9	88	44
	TURP	59	67	23.0	9.1	85	45
Wilson *et al.*, 2006[134]	Laser resection	30	71	26.0	8.4	113	78
	TURP	30	70	23.7	8.3	126	70

TURP, transurethral resection of the prostate.
Data given as mean values.
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association)

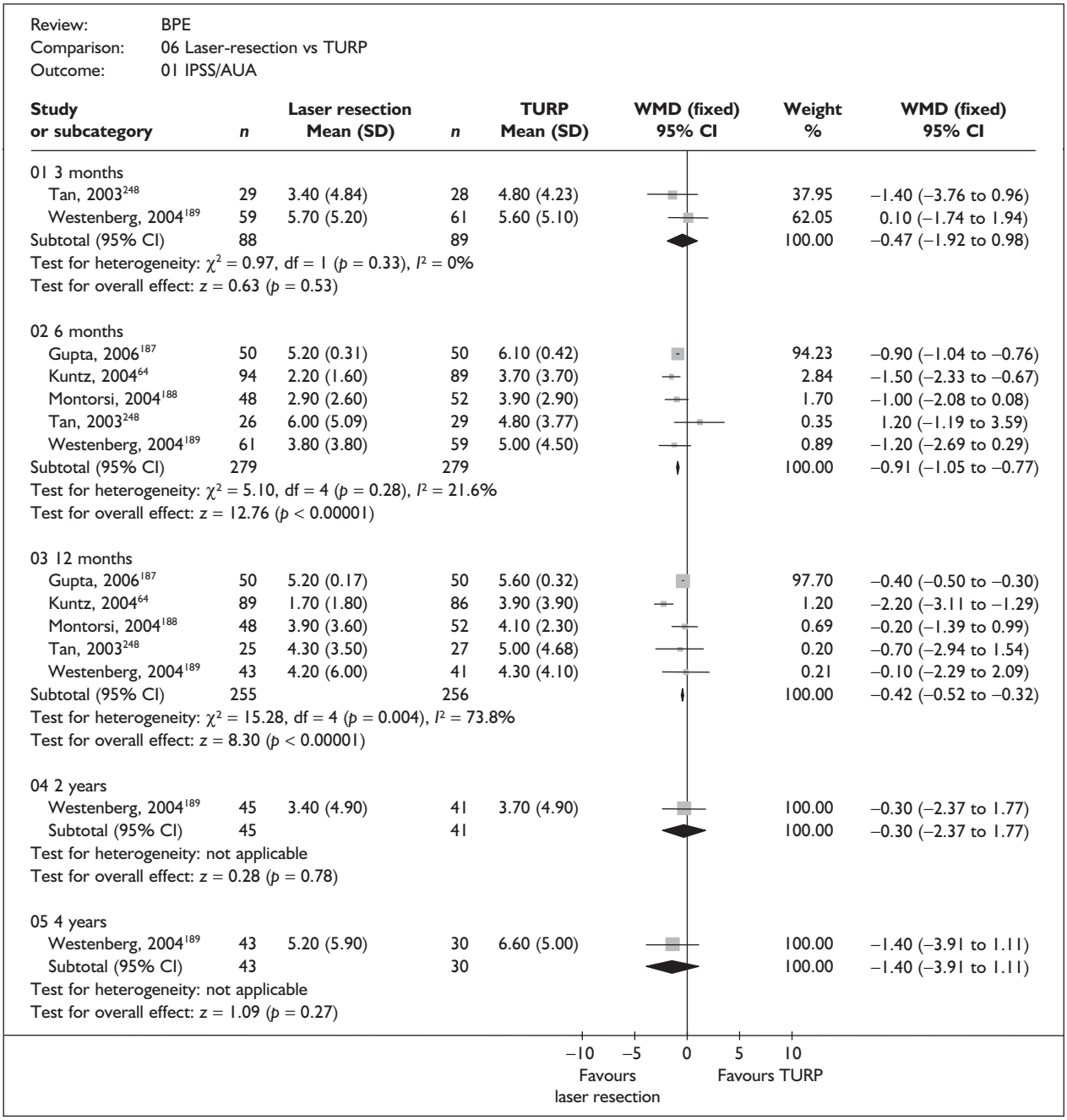


FIGURE 16 *Symptom scores, laser resection vs TURP.*

with a WMD of –0.42 (95% CI –0.52 to –0.32, $p < 0.00001$). As there appeared to be heterogeneity present in this comparison, a random-effects model was applied. The WMD still favoured laser resection; however, the difference was no longer statistically significant (WMD –0.80, 95% CI –1.70 to 0.10, $p = 0.08$).

Longer-term follow-up

Figure 16, comparison 06:01:05 shows data from the single trial that compared IPSS scores of patients who underwent laser resection and TURP at follow-up after 2 and 4 years. There were lower scores for laser resection technology as opposed to TURP at both follow-ups, although this was not statistically significant. However, losses to follow-up were high at both time periods (*Figure 16*, comparison 06:01:05: MD –1.40, 95% CI –3.91 to 1.11, $p = 0.27$).

Complications

Data describing complications by study are given in Appendix 8.6, *Table 68*. In total, 12 categories of complications were identified across the five

studies. These data are difficult to interpret. For seven of the complications, data were only available for one or two trials. Even for those complications more consistently reported, confidence intervals are wide and tend to include clinically important differences. Furthermore, the length of follow-up varied across the trials. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 17*). Results for other complications are presented in Appendix 9.6, comparison 06:02.

Blood transfusion

In a meta-analysis of five studies[64,187–189,248] patients allocated to laser resection were less likely to have a blood transfusion than those allocated to TURP (*Figure 17*, comparison 06:02:01: 1/293 versus 9/287, RR 0.27, 95% CI 0.07–0.95, $p = 0.04$).

Urinary retention

All five studies provided details on the incidence of urinary retention after surgery. There were 15 (5.1%) reports of urinary retention amongst 293 participants allocated laser resections versus 21 (7.3%) amongst 287 participants allocated to TURP. The direction of effect varied across studies and the difference was not statistically significant (*Figure 17*, comparison 06:02:02: RR 0.71, 95% CI 0.38–1.32, $p = 0.28$).

Urinary tract infection

There were five reports of urinary tract infection in each arm across two studies.[189,248] The direction of effect varied and the difference was not statistically significant (*Figure 17*, comparison 06:02:03: 5/91 versus 5/89, RR 0.98, 95% CI 0.31–3.09, $p = 0.97$).

Stricture

Strictures were reported in all five studies. There were no statistically significant differences between the two arms in terms of the incidence of strictures after surgery (*Figure 17*, comparison 06:02:04: 15/287 versus 17/273, RR 0.84, 95% CI 0.43–1.65, $p = 0.61$).

TUR syndrome

Out of the five eligible studies, only one reported TUR syndrome. There were no cases of a TUR syndrome amongst 52 patients randomised to laser resection. In the TURP arm, one event (2%) was recorded amongst 48 randomised patients (*Figure 17*, comparison 06:02:05: RR 0.31, 95% CI 0.01–7.39, $p = 0.47$).

Urinary incontinence

Meta-analysis of four trials[64,187–189] showed no difference in the risk of developing urinary incontinence following laser resection compared with the risk for those allocated to TURP (*Figure 17*, comparison 06:02:06: 55/252 versus 54/253, RR 0.97, 95% CI 0.72–1.31, $p = 0.83$). This result should be interpreted with caution as the length of follow-up varied and the type of incontinence was not fully described across studies.

Quality of life

Three studies[134,188,189] reported quality of life of patients following surgery. The quality of life was assessed using the IPSS QoL (0–6) questionnaire (*Figure 18*).

At 3 months

Meta-analysis of data from two studies[134,189] showed no statistically significant difference between holmium laser resection and TURP (*Figure 18*, comparison 06:08:01: WMD –0.19, 95% CI –0.68 to 0.30, $p = 0.45$).

At 12 months

At 12 months, evidence from three studies[134,188,189] showed marked heterogeneity present in the meta-analysis and the direction of effect was not consistent. In two studies the total number of participants available for quality of life evaluation was unclear and therefore this result should be treated with further caution.

Longer-term follow-up

Based on only one trial,[189] quality of life appeared to be similar in the laser group when compared with TURP at 2 and 4 years after surgery (*Figure 18*, comparison 06:08:06). A further caution is that the total number of participants available for this follow-up assessment was unclear.

Urodynamic outcomes

Data on peak urine flow rate, mean urine flow rate, residual volume, detrusor pressure and prostate size were reported to a varying extent across the five studies.[64,134,187–189] Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.6, *Table 69* and Appendix 9.6. comparisons 06:03–06:07.

At 3 months

Out of the total of five studies, two[134,189] reported peak urine flow rate at the 3-month follow-up.

Review: BPE
Comparison: 06 Laser resection vs TURP
Outcome: 02 Complications

Study or subcategory	Laser resection n/N	TURP n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 Blood transfusion					
Gupta, 2006[187]	0/50	1/50		13.50	0.33 (0.01–7.99)
Kuntz, 2004[64]	0/100	2/100		22.49	0.20 (0.01–4.11)
Montorsi, 2004[188]	1/52	1/48		9.36	0.92 (0.06–14.35)
Tan, 2003[248]	0/30	1/30		13.50	0.33 (0.01–7.87)
Westenberg, 2004[189]	0/61	4/59		41.15	0.11 (0.01–1.95)
Subtotal (95% CI)	293	287		100.00	0.27 (0.07–0.95)
Total events: 1 (Laser resection), 9 (TURP)					
Test for heterogeneity: $\chi^2 = 1.24$, df = 4 ($p = 0.87$), $I^2 = 0\%$					
Test for overall effect: $z = 2.05$ ($p = 0.04$)					
02 Urinary retention					
Gupta, 2006[187]	2/50	3/50		13.84	0.67 (0.12–3.82)
Kuntz, 2004[64]	0/100	5/100		25.38	0.09 (0.01–1.62)
Montorsi, 2004[188]	3/52	1/48		4.80	2.77 (0.30–25.73)
Tan, 2003[248]	5/30	4/30		18.46	1.25 (0.37–4.21)
Westenberg, 2004[189]	5/61	8/59		37.53	0.60 (0.21–1.74)
Subtotal (95% CI)	293	287		100.00	0.71 (0.38–1.32)
Total events: 15 (Laser resection), 21 (TURP)					
Test for heterogeneity: $\chi^2 = 4.33$, df = 4 ($p = 0.36$), $I^2 = 7.5\%$					
Test for overall effect: $z = 1.09$ ($p = 0.28$)					
03 Urinary tract infection					
Tan, 2003[248]	0/30	2/30		45.05	0.20 (0.01–4.00)
Westenberg, 2004[189]	5/61	3/59		54.95	1.61 (0.40–6.45)
Subtotal (95% CI)	91	89		100.00	0.98 (0.31–3.09)
Total events: 5 (Laser resection), 5 (TURP)					
Test for heterogeneity: $\chi^2 = 1.58$, df = 1 ($p = 0.21$), $I^2 = 36.7\%$					
Test for overall effect: $z = 0.04$ ($p = 0.97$)					
04 Stricture					
Gupta, 2006[187]	1/50	2/50		11.50	0.50 (0.05–5.34)
Kuntz, 2004[64]	6/95	2/88		11.94	2.78 (0.58–13.41)
Montorsi, 2004[188]	1/52	4/48		23.92	0.23 (0.03–1.99)
Tan, 2003[248]	1/29	3/28		17.55	0.32 (0.04–2.91)
Westenberg, 2004[189]	6/61	6/59		35.08	0.97 (0.33–2.83)
Subtotal (95% CI)	287	273		100.00	0.84 (0.43–1.65)
Total events: 15 (Laser resection), 17 (TURP)					
Test for heterogeneity: $\chi^2 = 4.58$, df = 4 ($p = 0.33$), $I^2 = 12.6\%$					
Test for overall effect: $z = 0.51$ ($p = 0.61$)					
05 TUR syndrome					
Montorsi, 2004[188]	0/52	1/48		100.00	0.31 (0.01–7.39)
Subtotal (95% CI)	52	48		100.00	0.31 (0.01–7.39)
Total events: 0 (Laser resection), 1 (TURP)					
Test for heterogeneity: not applicable					
Test for overall effect: $z = 0.73$ ($p = 0.47$)					
06 Incontinence					
Gupta, 2006[187]	1/50	1/50		1.81	1.00 (0.06–15.55)
Kuntz, 2004[64]	27/89	33/86		60.68	0.79 (0.52–1.20)
Montorsi, 2004[188]	26/52	18/48		33.84	1.33 (0.85–2.10)
Westenberg, 2004[189]	1/61	2/59		3.68	0.48 (0.05–5.19)
Subtotal (95% CI)	252	243		100.00	0.97 (0.72–1.31)
Total events: 55 (Laser resection), 54 (TURP)					
Test for heterogeneity: $\chi^2 = 3.15$, df = 3 ($p = 0.37$), $I^2 = 4.9\%$					
Test for overall effect: $z = 0.22$ ($p = 0.83$)					

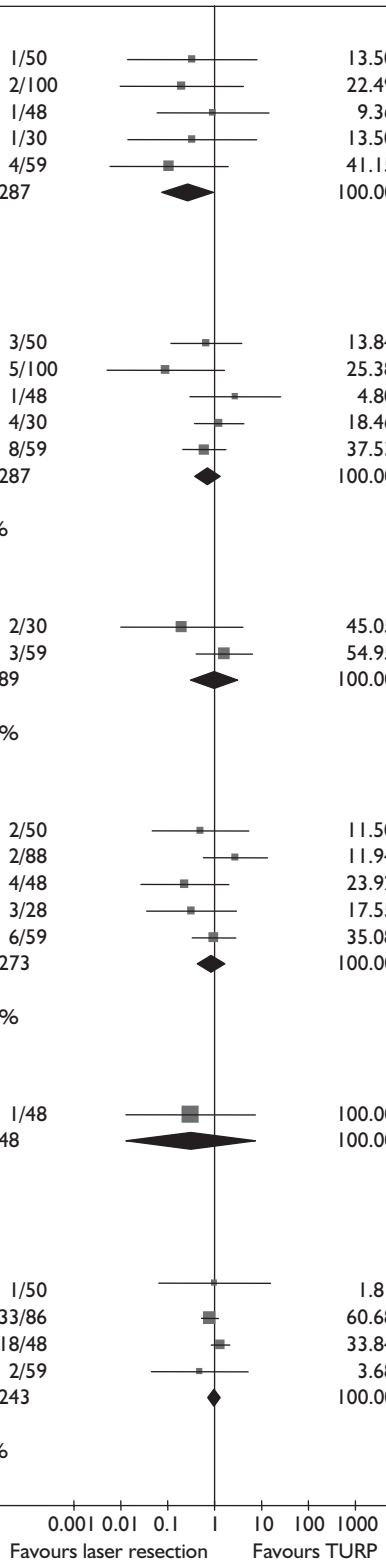


FIGURE 17 *Complications, laser resection vs TURP.*

Review: BPE
Comparison: 06 Laser resection vs TURP
Outcome: 09 Quality of life

Study or subcategory	n	Laser resection Mean (SD)	n	TURP Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Westenberg, 2004[189]	61	1.40 (1.50)	59	1.60 (1.40)		88.06	–0.20 (–0.72 to 0.32)
Wilson, 2006[134]	28	1.80 (2.10)	29	1.90 (3.23)		11.94	–0.10 (–1.51 to 1.31)
Subtotal (95% CI)	89		88			100.00	–0.19 (–0.68 to 0.30)
Test for heterogeneity: $\chi^2 = 0.02$, df = 1 ($p = 0.90$), $I^2 = 0\%$							
Test for overall effect: $z = 0.76$ ($p = 0.45$)							
02 6 months							
Montorsi, 2004[188]	52	1.00 (0.80)	48	0.60 (0.20)		75.92	0.40 (0.18–0.62)
Westenberg, 2004[189]	61	1.10 (1.30)	59	1.50 (1.40)		16.38	–0.40 (–0.88 to 0.08)
Wilson, 2006[134]	26	1.60 (1.53)	29	1.50 (1.07)		7.70	0.10 (–0.61 to 0.81)
Subtotal (95% CI)	139		136			100.00	0.25 (0.05–0.44)
Test for heterogeneity: $\chi^2 = 8.82$, df = 2 ($p = 0.01$), $I^2 = 77.3\%$							
Test for overall effect: $z = 2.46$ ($p = 0.01$)							
03 12 months							
Montorsi, 2004[188]	52	1.40 (0.90)	48	0.80 (1.28)		53.95	0.60 (0.16–1.04)
Westenberg, 2004[189]	61	0.88 (1.40)	59	1.60 (1.50)		38.17	–0.72 (–1.24 to –0.20)
Wilson, 2006[134]	25	1.50 (2.50)	27	1.40 (1.56)		7.88	0.10 (–1.04 to 1.24)
Subtotal (95% CI)	138		134			100.00	0.06 (–0.26 to 0.38)
Test for heterogeneity: $\chi^2 = 14.53$, df = 2 ($p = 0.0007$), $I^2 = 86.2\%$							
Test for overall effect: $z = 0.35$ ($p = 0.73$)							
04 18 months							
Westenberg, 2004[189]	61	0.72 (1.10)	59	1.30 (1.10)		100.00	–0.58 (–0.97 to –0.19)
Subtotal (95% CI)	61		59			100.00	–0.58 (–0.97 to –0.19)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 2.89$ ($p = 0.004$)							
05 2 years							
Westenberg, 2004[189]	45	0.98 (1.30)	41	1.00 (1.30)		50.44	–0.02 (–0.57 to 0.53)
Wilson, 2006[134]	22	1.25 (0.94)	26	1.25 (1.02)		49.56	0.00 (–0.55 to 0.55)
Subtotal (95% CI)	67		67			100.00	–0.01 (–0.40 to 0.38)
Test for heterogeneity: $\chi^2 = 0.00$, df = 1 ($p = 0.96$), $I^2 = 0\%$							
Test for overall effect: $z = 0.05$ ($p = 0.96$)							
06 4 years							
Westenberg, 2004[189]	43	1.10 (1.10)	30	1.40 (1.40)		100.00	–0.30 (–0.90 to 0.30)
Subtotal (95% CI)	43		30			100.00	–0.30 (–0.90 to 0.30)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 0.98$ ($p = 0.33$)							

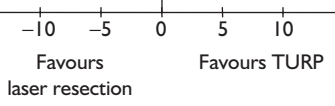


FIGURE 18 *Quality of life, laser resection vs TURP.*

Laser resection was associated with a higher peak urine flow rate (Appendix 9.6, comparison 06:03:01: WMD 3.49 ml/s, 95% CI 0.63–6.35, $p = 0.02$).

At 12 months

Again, meta-analysis of five studies[64,134,187–189] reporting peak urine flow rate showed higher peak urine flow rates for laser resection at 12 months after surgery (WMD 1.43, 95% CI 0.92–1.93, $p < 0.001$).

Longer-term follow-up

Only one study[189] reported peak urine flow rates at 4 years after the initial operation and this was based on about 60% of the original participants. No statistically significant difference was observed in this outcome between the two groups but the confidence interval was wide (Appendix 9.6, comparison 06:03:06: WMD 3.80, 95% CI –1.36 to 8.96, $p = 0.15$).

Descriptors of care

Data describing selected aspects of care are tabulated in Appendix 8.6, *Table 70*. Information on duration of operation, length of hospital stay and reoperation rates was identified across five eligible studies for this comparison.

Duration of operation

The duration of a laser resection intervention was found to be on average 17 minutes longer than a TURP intervention (Appendix 9.6, comparison 06:10: 95% CI 13.45–20.47, $p < 0.001$). The direction and size of effect were consistent across studies.

Length of hospital stay

Across the five studies the average length of stay was significantly shorter in the laser resection group than in the TURP group (Appendix 9.6, comparison 06:11: WMD –1.05 days, 95% CI –1.20 to –0.89, $p < 0.001$). The direction and size of effect were also consistent across studies.

Reoperation

Reoperations were reported in four trials.[64,188,189,248] No statistically significant differences were observed (Appendix 9.6, comparison 06:02:12: 10/231 versus 15/232, RR 0.68, 95% CI 0.32–1.44, $p = 0.31$).

Summary and conclusions of the evidence for and against the intervention

Five RCTs of moderate quality involving 580 participants were available to compare laser resection with TURP. In terms of symptom scores, laser resection appeared to be better than TURP; however, this difference was only statistically significant at 12 months when a complete data set involving all 580 participants was available. The data also indicate that peak urine flow rate was better after laser resection than after TURP at 3 and 12 months after the interventions. Although these results are statistically significant, the difference is small and therefore may not be clinically relevant. The rate of blood transfusion for laser resection was lower. The occurrence of urinary retention, urinary tract infection, stricture, TUR syndrome, urinary incontinence and reoperation was similar but with wide confidence intervals. Quality of life does not appear to differ between the two groups and there is good evidence that laser resection is associated with longer duration of operation but shorter length of hospital stay.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 17*. These should be interpreted in view of the comments mentioned earlier in this chapter.

Laser vaporisation versus TURP

Characteristics of included studies

The baseline characteristics of the included studies are summarised in *Table 18*. A total of 854 participants were randomised across 11 eligible RCTs reported in 27 papers.[121,127,141,146,148,153,164,179,190–193,249–263] The total number of people allocated to laser vaporisation was 425 and the total allocated to TURP was 429.

Three studies took place in the UK,[127,164,179] two each in the US[146,148] and Finland,[153,191] and one each in Australia,[141] France,[190] Turkey[192] and the Netherlands.[193] All but two studies[146,179] provided details on recruitment dates, with the earliest being January 1993[164] and the latest in January 2004.[141]

In terms of symptom scores, all but three studies[141,153,191] reported IPSS/AUA scores. Of the studies reporting baseline IPSS/AUA scores, 285 (84%) participants allocated to laser vaporisation had severe symptoms of BPE and 55 (16%) had moderate symptoms compared with 201 (59%) with severe and 155 (46%) with moderate symptoms allocated to TURP.

Of the studies reporting prostate size, 226 (57%) participants allocated to laser vaporisation had

TABLE 17 *Summary of the clinical effect sizes from meta-analyses, laser resection vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	2 (2)	–0.47[a]	–1.92 to 0.98	0.53
12 months	5 (5)	–0.42[a]	–0.5 to –0.32	< 0.001
Longer term	1 (1)	–1.40[a]	–3.9 to 1.11	0.27
Blood transfusion	5 (5)	0.27[b]	0.07–0.95	0.04
Urinary retention	5 (5)	0.71[b]	0.38–1.31	0.28
Urinary tract infection	2 (2)	0.98[b]	0.31–3.09	0.97
Stricture	5 (5)	0.84[b]	0.43–1.65	0.61
TUR syndrome	1 (1)	0.31[b]	0.01–7.39	0.47
Incontinence	4 (4)	0.97[b]	0.72–1.31	0.83
Quality of life				
3 months	2 (2)	–0.19[a]	–0.6 to 0.30	0.45
12 months	3 (3)	0.06[a]	–0.2 to 0.38	0.73
Longer term	1 (1)	–0.30[a]	–0.9 to 0.30	0.33
Q_{max}				
3 months	2 (2)	3.49[a]	0.63–6.35	0.02
12 months	5 (5)	1.43[a]	0.92–1.93	< 0.001
Longer term	1 (1)	3.80[a]	–1.3 to 8.96	0.15
Duration of operation	5 (5)	16.96[a]	13.45–20.47	< 0.001
Length of hospital stay	4 (4)	–1.05[a]	–1.2 to –0.89	< 0.001
Reoperation	4 (4)	0.68[b]	0.32–1.44	0.31

IPSS/AUA, International Prostate Symptom Score/American Urological Association MA, meta-analysed; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

large prostates, 112 (28%) had moderate-sized prostates and 10 (2%) had small prostates. In the TURP arm, 200 (51%) had large prostates, 113 (29%) had moderate-sized prostates and 86 (22%) had small prostates.

Assessment of effectiveness

As discussed in Chapter 2 there are several laser devices that can be used to vaporise the prostate. The most commonly used are Nd:YAG, holmium:YAG and KTP lasers. These can be used either alone or in combination (hybrid laser). For analysis purposes, trials reporting a vaporisation technique were combined, regardless of the method/devices used.

Symptom scores

At 3 months

Of the 11 eligible studies, only five provided details on IPSS/AUA scores at 3 months following surgery.[146,164,179,190,192] Meta-analysis of three of these trials[164,179,192] is marked by considerable heterogeneity in which the direction of effect and effect sizes vary across studies with one study favouring TURP.[164] The source of heterogeneity is unclear; however, it may be due to different levels of energy delivery across studies. Moreover, there is variation in the prostate size of patients measured before surgery. On average, patients included in the Oxford laser trial[164] exhibited large prostates whereas those included in the trial by Suvakovic and Hindmarsh had small prostates.[179] Sengor and

TABLE 18 *Summary of the baseline characteristics, laser vaporisation vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Bouchier-Hayes *et al.*, 2006[141]	Laser vaporisation	38	65	NR	NR	NR	42
	TURP	38	66	NR	NR	NR	33
Carter *et al.*, 1999[127]	Laser vaporisation	95	68	20.3	9.0	109	42
	TURP	96	67	19.8	9.5	135	42
Keoghane *et al.*, 2000[164]	Laser vaporisation	72	69	19.9	11.8	NR	55
	TURP	79	70	19.4	11.4	NR	52
Mottet *et al.*, 1999[190]	Laser vaporisation	17	64	21.7	8.8	NR	37
	TURP	13	67	23.7	7.7	NR	34
Sengor *et al.*, 1996[192]	Laser vaporisation	30	61	21.8	8.7	110	NR
	TURP	30	66	22.1	8.4	155	NR
Shingleton *et al.*, 2002[146]	Laser vaporisation	50	68	22	NR	NR	32
	TURP	50	67	21	NR	NR	30
Suvakovic and Hindmarsh, 1996[179]	Laser vaporisation	10	63	18.0	12.2	140	24
	TURP	10	66	18.8	11.1	162	22
Tuhkanen *et al.*, 2001[191]	Laser vaporisation	21	67[b]	23[b,c]	7.2	138	55
	TURP	25	67[b]	19[b,c]	8.5	125	55
Tuhkanen *et al.*, 2003[153]	Laser vaporisation	26	68[b]	18[b,c]	8.3[b]	87[b]	30[b]
	TURP	26	67[b]	18[b,c]	8.6[b]	83[b]	28[b]
van Melick *et al.*, 2003[193]	Laser vaporisation	45	67	18.9	12.0	300	37
	TURP	50	66	16.8	11.0	350	37
Zorn *et al.*, 1999[148]	Laser vaporisation	21	71	24.0	8.7	NR	30
	TURP	12	69	24.7	9.0	NR	34

NR, not reported; TURP, transurethral resection of the prostate.
Data given as mean values (unless stated otherwise).
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association) unless stated otherwise.
b Median.
c Danish Prostatic Symptom Score (Dan PSS1).

colleagues[192] did not provide details on baseline prostate size.

At 12 months

At 12 months, all but one study[193] out of eight favoured TURP. Pooling the data of three studies amenable to meta-analysis showed statistically significant better IPSS/AUA scores in support of TURP. However, confidence intervals were wide, there was evidence of heterogeneity and the trials included a small number of participants (*Figure 19*, comparison 07:01:03: WMD 1.30, 95% CI 0.12–2.47, $p = 0.03$).

Longer-term follow-up

At 5 years, combining data from three trials gave higher (poorer) scores for laser vaporisation than for TURP (*Figure 19*, comparison 07:01:06: WMD 2.42, 95% CI 0.08–4.75, $p = 0.04$).

Complications

Data describing complications by study are given in Appendix 8.7, *Table 72*. Information from one or more of the 11 trials was available for 17 complications. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are

presented in this section (*Figure 20*). Results for other complications are presented in Appendix 9.7, comparison 07:02. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied.

Blood transfusion
In the ten studies[127,141,146,148,153,164,190–193] that reported blood transfusion there was only one transfusion amongst 374 laser patients versus 24 amongst 415 TURP patients (*Figure 20*, comparison 07:02:01: RR 0.14, 95% CI 0.05–0.42, $p = 0.0004$).

Urinary retention
In six studies [127,146,164,190,191,193] a total of 32 (10.5%) cases of urinary retention amongst 304 patients allocated to laser vaporisation versus 11 (3.6%) cases amongst 306 TURP patients were reported (*Figure 20*, comparison 07:02:02: RR 2.89, 95% CI 1.55–5.42, $p = 0.0009$).

Urinary tract infection
Meta-analysis of data from four studies[127,153,164,193] indicated fewer episodes of urinary tract infection following TURP with an RR of 1.63 (95% CI 0.99–2.69, $p = 0.05$). However, this result depends entirely on data from the study by Carter and colleagues,[127] as epididymitis and prostatitis are reported as well as simple urinary tract infections that occurred in the early postoperative period. When only epididymitis and prostatitis are considered, the difference in rates observed in the laser vaporisation and TURP groups is no longer statistically significant (RR 1.17, 95% CI 0.60–2.26, $p = 0.32$).

Strictures
The incidence of strictures for those who underwent laser vaporisation and TURP was available from nine studies.[127,141,146,153,164,190–193] The proportion of people who developed strictures appeared to be lower following laser vaporisation than following TURP. The pooled RR of strictures among laser patients compared with TURP patients was 0.54 (*Figure 20*, comparison 07:02:04: 13/350 versus 27/353, 95% CI 0.32–0.90, $p = 0.02$). It should be noted that eight of the 13 strictures and 11 of the 27 strictures observed in the laser vaporisation and TURP groups, respectively, were actually bladder neck contractures.

TUR syndrome
There were no cases of TUR syndrome amongst 161 patients allocated to laser vaporisation compared with one amongst 122 patients allocated to TURP (*Figure 20*, comparison 07:02:05: RR 0.33, 95% CI 0.01–7.93, $p = 0.50$).

Incontinence
Taken together, data from five trials suggest a higher rate of incontinence following laser vaporisation (*Figure 20*, comparison 07:02:06: 16/272 versus 7/285, RR 2.24, 95% CI 1.03–4.88, $p = 0.04$). However, this result depended on a single trial[193] in which rates were high in both groups but particularly following laser vaporisation. This result should also be treated with caution because the length of follow-up varied and the definition of incontinence was not fully described in the studies.

Quality of life
Three studies[193,249,250] using a variety of methods reported quality of life of patients following surgery (Appendix 8.7, *Table 73*). In one study[193] the quality of life was assessed using the disease-specific IPSS QoL (0–6) questionnaire. In another study[249] the generic quality of life measure Medical Outcomes Study 36-item Short Form Health Study (SF-36) was used. In the third study[250] quality of life was measured using two distinct instruments: SF-36 and EuroQol Five Dimensions (EQ-5D) (scored using the UK tariffs).

At 3 months there appeared to be little change in quality of life as a consequence of either surgical intervention, irrespective of which quality of life tool was used.[250] No differences in quality of life were detected in two studies[193,250] at 12 months.

Urodynamic outcomes
Data on peak urine flow rate, mean urine flow rate, residual volume, detrusor pressure and prostate size were reported to a varying extent across eight studies.[127,146,148,153,164,190–192] Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.7, *Table 74* and Appendix 9.7, comparisons 07:04–07:08.

At 3 months
Six studies[146,153,164,190–192] provided details on peak urine flow rate for patients at 3 months after surgery. Only four,[146,153,164,192] however, presented data that were sufficiently similar to allow quantitative synthesis. The WMD was 1.76 ml/s, lower (worse) for laser vaporisation (Appendix 9.7, comparison 07:04:01: 95% CI 0.57–2.94, $p = 0.004$). This result was consistent with that reported by Tuhkanen and colleagues[191] but not with the small study reported by Mottet and colleagues.[190]

Review: BPE
Comparison: 07 Laser vaporisation vs TURP
Outcome: 01 IPSS/AUA

Study or subcategory	n	Laser vaporisation Mean (SD)	n	TURP Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Keoghane, 2000[164]	55	9.60 (7.50)	62	6.50 (5.10)		34.07	3.10 (0.75–5.45)
Sengor, 1996[192]	30	8.50 (4.20)	30	9.80 (3.10)		54.10	−1.30 (−3.17 to 0.57)
Suvakovic, 1996[197]	10	9.70 (2.60)	10	12.80 (5.90)		11.82	−3.10 (−7.10 to 0.90)
Subtotal (95% CI)	95		102			100.00	−0.01 (−1.39 to 1.36)
Test for heterogeneity: $\chi^2 = 10.84$, df = 2 ($p = 0.004$), $I^2 = 81.5\%$							
Test for overall effect: $z = 0.02$ ($p = 0.98$)							
02 6 months							
van Melick, 2003a[193]	33	5.90 (5.50)	37	3.20 (2.70)		37.90	2.70 (0.63 – 4.77)
Sengor, 1996[192]	30	7.80 (2.60)	30	9.30 (4.20)		51.90	−1.50 (−3.27 to 0.27)
Suvakovic, 1996[197]	9	8.70 (5.40)	10	8.50 (3.00)		10.20	0.20 (−3.79 to 4.19)
Subtotal (95% CI)	72		77			100.00	0.27 (−1.01 to 1.54)
Test for heterogeneity: $\chi^2 = 9.16$, df = 2 ($p = 0.01$), $I^2 = 78.2\%$							
Test for overall effect: $z = 0.41$ ($p = 0.68$)							
03 12 months							
Keoghane, 2000[164]	52	8.87 (6.51)	60	5.77 (5.40)		27.67	3.10 (0.86–5.34)
van Melick, 2003a[193]	37	3.60 (3.40)	41	4.10 (4.80)		41.16	−0.50 (−2.33 to 1.33)
Shingleton, 2002[146]	40	6.00 (6.00)	33	3.80 (4.10)		25.54	2.20 (−0.13 to 4.53)
Suvakovic, 1996[197]	9	8.70 (4.90)	10	7.20 (6.10)		5.63	1.50 (−3.45 to 6.45)
Subtotal (95% CI)	138		144			100.00	1.30 (0.12–2.47)
Test for heterogeneity: $\chi^2 = 6.78$, df = 3 ($p = 0.08$), $I^2 = 55.7\%$							
Test for overall effect: $z = 2.16$ ($p = 0.03$)							
04 2 years							
Keoghane, 2000[164]	45	7.80 (6.60)	52	5.70 (6.00)		58.51	2.10 (−0.43 to 4.63)
Shingleton, 2002[146]	23	5.90 (5.70)	19	4.60 (4.20)		41.49	1.30 (−1.70 to 4.30)
Subtotal (95% CI)	68		71			100.00	1.77 (−0.16 to 3.70)
Test for heterogeneity: $\chi^2 = 0.16$, df = 1 ($p = 0.69$), $I^2 = 0\%$							
Test for overall effect: $z = 1.79$ ($p = 0.07$)							
05 4 years							
van Melick, 2003a[193]	10	9.30 (5.20)	15	5.80 (7.50)		100.00	3.50 (−1.48 to 8.48)
Subtotal (95% CI)	10		15			100.00	3.50 (−1.48 to 8.48)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 1.38$ ($p = 0.17$)							
06 5 years							
Keoghane, 2000[164]	25	9.70 (7.50)	32	7.00 (5.70)		43.35	2.70 (−0.84 to 6.24)
Shingleton, 2002[146]	29	9.90 (6.70)	33	7.70 (5.60)		56.65	2.20 (−0.90 to 5.30)
Subtotal (95% CI)	54		65			100.00	2.42 (0.08–4.75)
Test for heterogeneity: $\chi^2 = 0.04$, df = 1 ($p = 0.84$), $I^2 = 0\%$							
Test for overall effect: $z = 2.03$ ($p = 0.04$)							
07 7 years							
van Melick, 2003a[193]	17	8.30 (6.40)	15	7.30 (7.10)		100.00	1.00 (−3.71 to 5.71)
Subtotal (95% CI)	17		15			100.00	1.00 (−3.71 to 5.71)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 0.42$ ($p = 0.68$)							

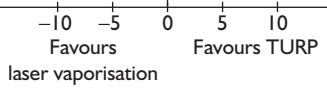


FIGURE 19 *Symptom scores, laser vaporisation vs TURP.*

Review: BPE
Comparison: 07 Laser vaporisation vs TURP
Outcome: 02 Complications

Study or subcategory	Laser vaporisation *n/N*	TURP *n/N*	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 Blood transfusion					
Bouchier-Hayes, 2006[283]	0/38	1/38		5.79	0.33 (0.01–7.93)
Carter, 1999[127]	0/95	5/96		21.12	0.09 (0.01–1.64)
Keoghane, 2000[164]	0/72	13/76		50.73	0.04 (0.00–0.65)
van Melick, 2003a[193]	0/45	1/50		5.49	0.37 (0.02–8.85)
Mottet, 1999[190]	0/23	0/13			Not estimable
Sengor, 1996[192]	0/30	2/30		9.65	0.20 (0.01–4.00)
Shingleton, 2002[146]	0/50	0/50			Not estimable
Tuhkanen, 2001[191]	1/21	2/24		7.21	0.57 (0.06–5.86)
Tuhkanen, 2003[153]	0/26	0/26			Not estimable
Zorn, 1999[148]	0/12	0/12			Not estimable
Subtotal (95% CI)	412	415		100.00	0.14 (0.05–0.42)
Total events: 1 (Laser vaporisation), 24 (TURP)					
Test for heterogeneity: $\chi^2 = 2.99$, df = 5 ($p = 0.70$), $I^2 = 0\%$					
Test for overall effect: $z = 3.51$ ($p = 0.0004$)					
02 Urinary retention					
Carter, 1999[127]	5/93	2/92		17.15	2.47 (0.49–12.43)
Keoghane, 2000[164]	17/72	8/76		66.37	2.24 (1.03–4.87)
van Melick, 2003a[193]	5/45	0/50		4.04	12.20 (0.69–214.56)
Mottet, 1999[190]	0/23	0/13			Not estimable
Shingleton, 2002[146]	3/50	1/50		8.53	3.00 (0.32–27.87)
Tuhkanen, 2001[191]	2/21	0/25		3.91	5.91 (0.30–116.66)
Subtotal (95% CI)	304	306		100.00	2.89 (1.55–5.42)
Total events: 32 (Laser vaporisation), 11 (TURP)					
Test for heterogeneity: $\chi^2 = 1.64$, df = 4 ($p = 0.80$), $I^2 = 0\%$					
Test for overall effect: $z = 3.32$ ($p = 0.0009$)					
03 Urinary tract infection					
Carter, 1999[127]	11/93	6/92		39.72	1.81 (0.70–4.70)
Keoghane, 2000[164]	2/72	3/76		19.22	0.70 (0.12–4.09)
van Melick, 2003a[193]	4/45	5/50		31.19	0.89 (0.25–3.11)
Tuhkanen, 2003[153]	0/26	1/26		9.88	0.33 (0.01–7.82)
Subtotal (95% CI)	236	244		100.00	1.17 (0.60–2.26)
Total events: 17 (Laser vaporisation), 15 (TURP)					
Test for heterogeneity: $\chi^2 = 1.93$, df = 3 ($p = 0.59$), $I^2 = 0\%$					
Test for overall effect: $z = 0.46$ ($p = 0.65$)					
04 Strictures					
Bouchier-Hayes, 2006[283]	5/38	8/38		21.49	0.63 (0.22–1.74)
Carter, 1999[127]	7/84	15/85		40.06	0.47 (0.20–1.10)
Keoghane, 2000[164]	0/72	5/76		14.38	0.10 (0.01–1.70)
van Melick, 2003a[193]	2/45	2/50		5.09	1.11 (0.16–7.56)
Mottet, 1999[190]	0/23	2/13		8.48	0.12 (0.01–2.26)
Sengor, 1996[192]	0/30	0/30			Not estimable
Shingleton, 2002[146]	4/50	1/50		2.69	4.00 (0.46–34.54)
Tuhkanen, 2001[191]	0/21	1/24		3.77	0.38 (0.02–8.83)
Tuhkanen, 2003[153]	0/25	1/25		4.03	0.33 (0.01–7.81)
Subtotal (95% CI)	388	391		100.00	0.54 (0.32–0.90)
Total events: 18 (Laser vaporisation), 35 (TURP)					
Test for heterogeneity: $\chi^2 = 6.59$, df = 7 ($p = 0.47$), $I^2 = 0\%$					
Test for overall effect: $z = 2.35$ ($p = 0.02$)					
05 TUR syndrome					
Bouchier-Hayes, 2006[283]	0/38	1/38		100.00	0.33 (0.01–7.93)
Carter, 1999[127]	0/93	0/92			Not estimable
Sengor, 1996[192]	0/30	0/30			Not estimable
Subtotal (95% CI)	161	160		100.00	0.33 (0.01–7.93)
Total events: 0 (Laser vaporisation), 1 (TURP)					
Test for heterogeneity: not applicable					
Test for overall effect: $z = 0.68$ ($p = 0.50$)					
06 Incontinence					
Carter, 1999[127]	1/84	0/85		6.10	3.04 (0.13–73.47)
Keoghane, 2000[164]	0/72	1/76		17.91	0.35 (0.01–8.49)
van Melick, 2003a[193]	14/45	4/50		46.49	3.89 (1.38–10.95)
Shingleton, 2002[146]	1/50	1/50		12.27	1.00 (0.06–15.55)
Tuhkanen, 2001[191]	0/21	1/24		17.23	0.38 (0.02–8.83)
Subtotal (95% CI)	272	285		100.00	2.24 (1.03–4.88)
Total events: 16 (Laser vaporisation), 7 (TURP)					
Test for heterogeneity: $\chi^2 = 3.98$, df = 4 ($p = 0.41$), $I^2 = 0\%$					
Test for overall effect: $z = 2.04$ ($p = 0.04$)					

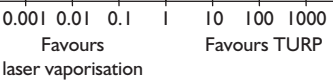


FIGURE 20 *Complications, laser vaporisation vs TURP.*

At 12 months

Five studies[127,146,148,164,190] provided details on peak urine flow rate at 12 months after surgery. Only two,[146,164] however, presented data that were sufficiently similar to allow quantitative synthesis. The WMD was 2.02 ml/s, lower (worse) for laser vaporisation (Appendix 9.7, comparison 07:04:03: 95% CI 0.71–4.75, $p = 0.15$). With regard to the studies in which data were not amenable to meta-analysis, two[127,148] favoured TURP and one[190] favoured laser vaporisation.

Longer-term follow-up

Meta-analysis of data from two[146,164] studies reporting 5-year data showed no statistically significant difference between the two groups (Appendix 9.7, comparison 07:04:06: WMD 0.28, 95% CI 1.76–2.32, $p = 0.79$). Loss to follow-up was high in both trials.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.7, *Table 75*. Information on duration of operation, length of hospital stay and reoperation rates was identified across the eligible studies for this comparison.

Duration of operation

A total of nine studies[127,148,153,164,179,190–193] provided information on duration of operation. In three studies[164,179,192] the mean duration of operation was shorter in the laser group and in one[193] there were no differences between the two groups. Meta-analysis of four studies with suitable data showed a non-statistically significant difference between laser vaporisation and TURP (Appendix 9.7, comparison 07:11: WMD 0.29, 95% CI –2.19 to 2.78, $p = 0.82$).

Length of hospital stay

Length of hospital stay was reported in eight studies, with six favouring the laser vaporisation group and two favouring TURP.[153,191] Only one study reported means and standard deviations[141,193] and meta-analysis suggested that there was no evidence of a difference between the two groups (Appendix 9.7, comparison 07:12).

Reoperations

Reoperations were reported in nine trials.[141,146,148,153,164,190,191,193,249] Reoperation was more common in the laser vaporisation group (9.3%) than in the TURP groupt (5.4%) (Appendix 9.7, comparison 07:03:17: RR 1.60, 95% CI 0.97–2.63, $p = 0.06$). It should be noted that differences between studies in timing and completeness of follow-up might have introduced bias.

Summary and conclusions of the evidence for and against the intervention

A total of 854 participants were randomised across 11 eligible studies of generally moderate quality. At 12 months or longer, the data indicated that symptom scores were worse after laser vaporisation than after TURP. There was a tendency for peak urine flow rate to favour TURP but this was only statistically significant at the 3- and 12-month follow-up assessments. The differences observed for both symptom scores and peak urine flow rate, although statistically significant, may not be clinically relevant or appreciable by patients. The occurrence of complications such as urinary retention, urinary tract infection and incontinence was higher for laser vaporisation than for TURP. However, blood transfusion and the incidence of strictures were lower. The duration of operation and length of hospital stay did not appear to differ between the two approaches.

The results for symptom scores displayed significant heterogeneity and there was a lack of consistency in the direction and size of effect across studies. Much of the variation might be due to differences in the specific aims and objectives of the trials.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 19*. These should be interpreted in view of all of the comments mentioned earlier in this chapter.

Interventions using non-laser technology

Transurethral vaporesection of the prostate (TUVRP) versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 20*. Five RCTs[68,132,187,202,203] were eligible for this comparison, randomising a total of 271 men to TUVRP and 258 to TURP.

Single studies took place in India,[187] Taiwan,[132] Turkey,[203] Saudi Arabia[68] and Germany.[202] Three studies provided details of recruitment dates[132,187,203]

with the earliest in November 1997[203] and the latest in December 2003.[187]

In terms of baseline IPSS/AUA scores, the total numbers of participants with moderate and severe symptoms who were allocated to TUVRP were 93 (34%) and 178 (66%) respectively. The equivalent figures in the TURP group were 142 (55%) and 116 (45%).

All studies reported prostate size, with all 529 participants having large prostates.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.8. The results of the meta-analyses are given in Appendix 9.8. Note that in terms of long-term evaluation, only the longest follow-up is presented.

Symptom scores

At 3 months

At 3 months after surgery, IPSS/AUA scores were reported in three of the five eligible studies.[132,202,203] Two of the three studies reported no statistically significant differences between TUVRP and TURP (Appendix 8.8, *Table 76*), whereas in the third study, reporting means and standard deviations, the mean difference was 0.30 (*Figure 21*, comparison 08:01:01: 95% CI 0.63–1.23, $p = 0.53$).

At 12 months

Evidence from two studies showed no statistically significant differences in IPSS/AUA scores at 12 months after TUVRP and TURP (*Figure 21*, comparison 08:01:03: WMD –0.59, 95% CI –1.40 to 0.23, $p = 0.16$).

TABLE 19 *Summary of the clinical effect sizes from meta-analyses, laser vaporisation vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	3 (8)	–0.01[a]	–1.39 to 1.36	0.98
12 months	4 (9)	1.30[a]	0.12–2.47	0.03
Longer term	2 (3)	2.42[a]	0.08–4.75	0.04
Blood transfusion	10 (10)	0.14[b]	0.05–0.42	< 0.001
Urinary retention	6 (6)	2.89[b]	1.55–5.42	< 0.001
Urinary tract infection	4 (4)	1.63[b]	0.99–2.69	0.05
Stricture	9 (9)	0.54[b]	0.32–0.90	0.02
TUR syndrome	3 (3)	0.33[b]	0.01–7.93	0.50
Incontinence	5 (5)	2.24[b]	1.03–4.88	0.04
Quality of life				
3 months	0 (2)	NR	NR	NR
12 months	1 (3)	0.00[a]	–0.40 to 0.40	1.00
Longer term	1 (1)	0.10[a]	–0.77 to 0.97	0.82
Q_{max}				
3 months	4 (6)	–1.76[a]	–2.94 to –0.57	0.004
12 months	2 (5)	–2.02[a]	–4.75 to 0.71	0.15
Longer term	2 (3)	–0.28[a]	–2.32 to 1.76	0.79
Duration of operation	4 (9)	0.29[a]	–2.19 to 2.78	0.82
Length of hospital stay	2 (9)	–1.39[a]	–1.69 to –1.10	< 0.001
Reoperation	9 (9)	1.68[b]	1.03–2.74	0.04

IPSS/AUA, International Prostate Symptom Score/American Urological Association MA, meta-analysed, NR, not reported; TUR, transurethral resection; TURP, transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

TABLE 20 *Summary of the baseline characteristics, TUVRP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Helke *et al.*, 2001[202]	TUVRP	93	69	17.3	10.8	76	49
	TURP	92	67	18.3	8.5	102	50
Kupeli *et al.*, 2001[203]	TUVRP	50	61	21.6	9.2	NR	57
	TURP	50	59	19.4	7.9	NR	58
Gupta *et al.*, 2006[187]	TUVRP	50	68	24.9	4.6	103	63
	TURP	50	66	23.3	4.5	84	60
Liu *et al.*, 2006[132]	TUVRP	44	66	25.6	6.9	131	58
	TURP	32	65	26.8	6.9	142	60
Talic *et al.*, 2000[68]	TUVRP	34	71	24.9	7.5	NR	57
	TURP	34	70	20.1	9.1	NR	52

NR, not reported; TURP, transurethral resection of the prostate; TUVRP, transurethral vaporesection of the prostate.
Data given as mean values.
a Symptom scores given as IPSS/AUA, International Prostate Symptom Score/American Urological Association.

Longer-term follow-up

IPSS/AUA scores at 2 years after surgery were provided in one trial. Again, no statistically significant differences were observed between TUVRP and TURP (*Figure 21*, comparison 08:01:04: WMD 0.60, 95% CI –1.09 to 2.29, $p = 0.49$).

Complications

The list of complications by study is detailed in Appendix 8.8, *Table 77*. Data describing 12 types of complications were variably reported across the five studies. The data were too few to provide precise estimates of differences and all confidence intervals were wide, such that clinically important differences could not be ruled out. None of the complications proved to be significantly different between TUVRP and TURP. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 22*). Results for other complications are presented in Appendix 9.8, comparison 08:02.

Blood transfusion

All five trials provided information on blood transfusions.[68,132,187,202,203] A total of seven (2.3%) patients required a blood transfusion following TUVRP as opposed to 12 (4.6%) patients following TURP (*Figure 22*, comparison 08:02:01: RR 0.57, 95% CI 0.24–1.36, $p = 0.20$).

Urinary retention

There were six cases of urinary retention amongst 144 patients randomised to TUVRP versus seven cases of urinary retention amongst 132 patients randomised to TURP (*Figure 22*, comparison 08:02:02: RR 0.72, 95% CI 0.26–2.05, $p = 0.54$).[132,187,203]

Urinary tract infection

No studies reported this outcome.

Stricture

Four studies[132,187,202,203] reported the incidence of strictures postoperatively. Meta-analysis showed no statistically significant differences between TUVRP and TURP (*Figure 22*, comparison 08:02:03: 9/229 versus 11/218, RR 0.75, 95% CI 0.32–1.77, $p = 0.51$).

TUR syndrome

There were no cases of a TUR syndrome in the TUVRP arm amongst 128 patients across three studies[68,132,203] compared with two (7%) events following TURP.

Urinary incontinence

Incontinence was reported in four studies.[132,187,202,203] There were 15 and 17 reports of incontinence amongst 229 and 218 patients allocated to TUVRP and TURP respectively (*Figure 22*, comparison 08:02:05, RR 0.85, 95% CI 0.45–1.61, $p = 0.62$).

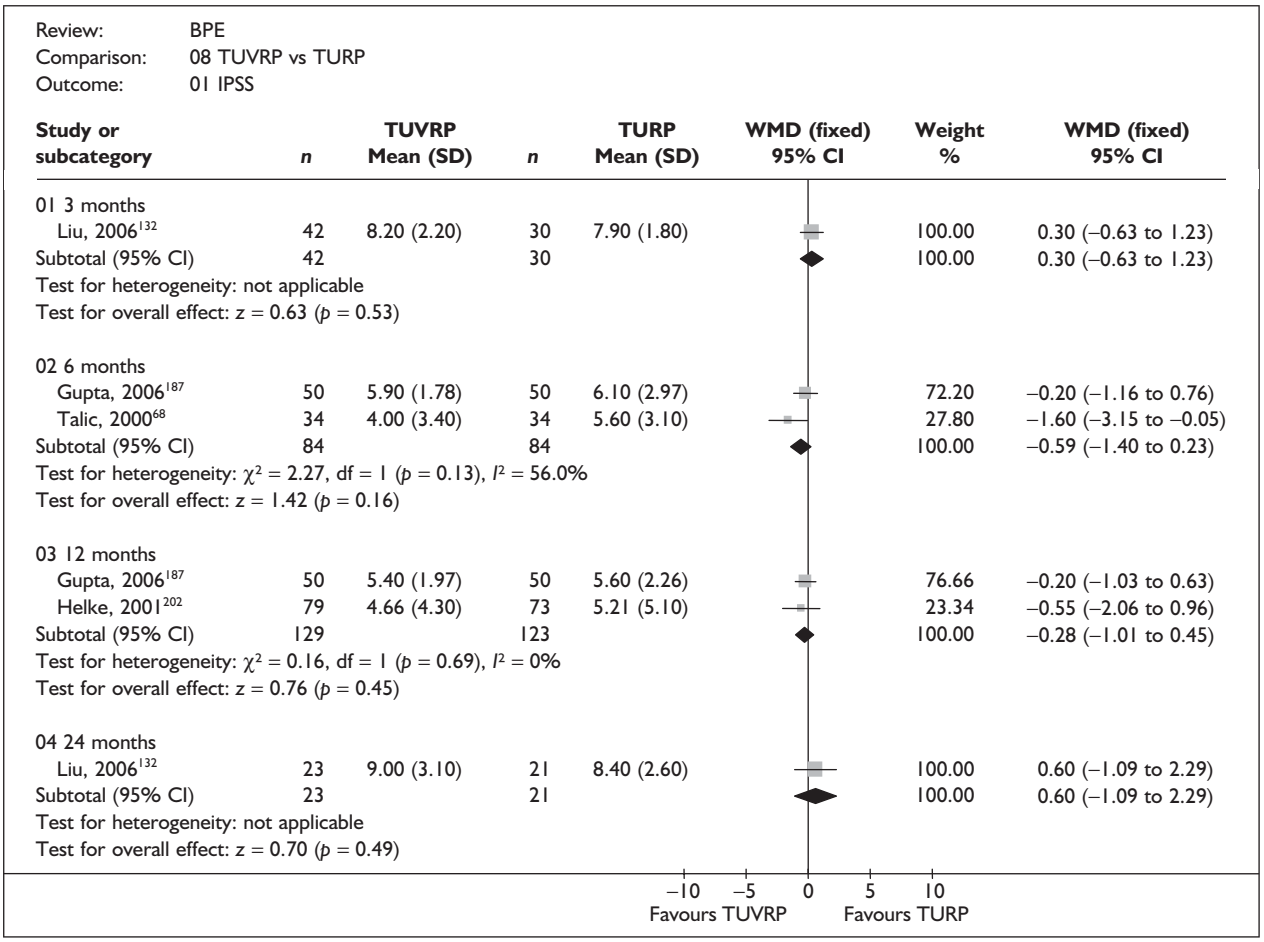


FIGURE 21 *Symptom scores, TUVRP vs TURP.*

Quality of life

Only one study[132] reported quality of life of patients following TUVRP or TURP (Appendix 8.8, *Table 78*). Quality of life was assessed using the IPSS QoL (0–6) questionnaire. At 3 months and 2 years there appeared to be little difference in quality of life between the groups as a consequence of either surgical intervention (Appendix 9.8, comparison 08:05).

Urodynamic outcomes

Data on peak urine flow rate and prostate size were reported across five studies.[68,132,187,202,203] These are tabulated in Appendix 8.8, *Table 79*. Only peak urine flow rate is presented in this section.

At 3 months

Two studies[132,202] provided details on peak urine flow rate for patients at 3 months after surgery. In one trial[132] the mean difference was 0.90 ml/s for TUVRP versus TURP (Appendix 9.8, comparison 08:03:01: 95% CI –0.04 to 1.84, $p = 0.06$). Helke and colleagues[202] reported a non-statistically significant difference between the two groups.

At 12 months

Two studies[187,202] provided details on peak urine flow rate at 12 months after surgery. The WMD was 0.10 ml/s for TUVRP versus TURP (Appendix 9.8, comparison 08:03:03: 95% CI –0.41 to 0.61, $p = 0.70$).

Longer-term follow-up

One study[132] provided results beyond 12 months (2 years). At this time point there was a non-statistically significant difference between TUVRP and TURP (Appendix 9.8, comparison 08:03:04: WMD 1.60, 95% CI –0.30 to 3.50, $p = 0.10$).

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.8, *Table 80*. Information on duration of operation, length of hospital stay and reoperation rates was identified to a varying extent across the five eligible studies for this comparison.

Duration of operation

Three studies[68,132,187] provided information on the duration of operation. The results were not

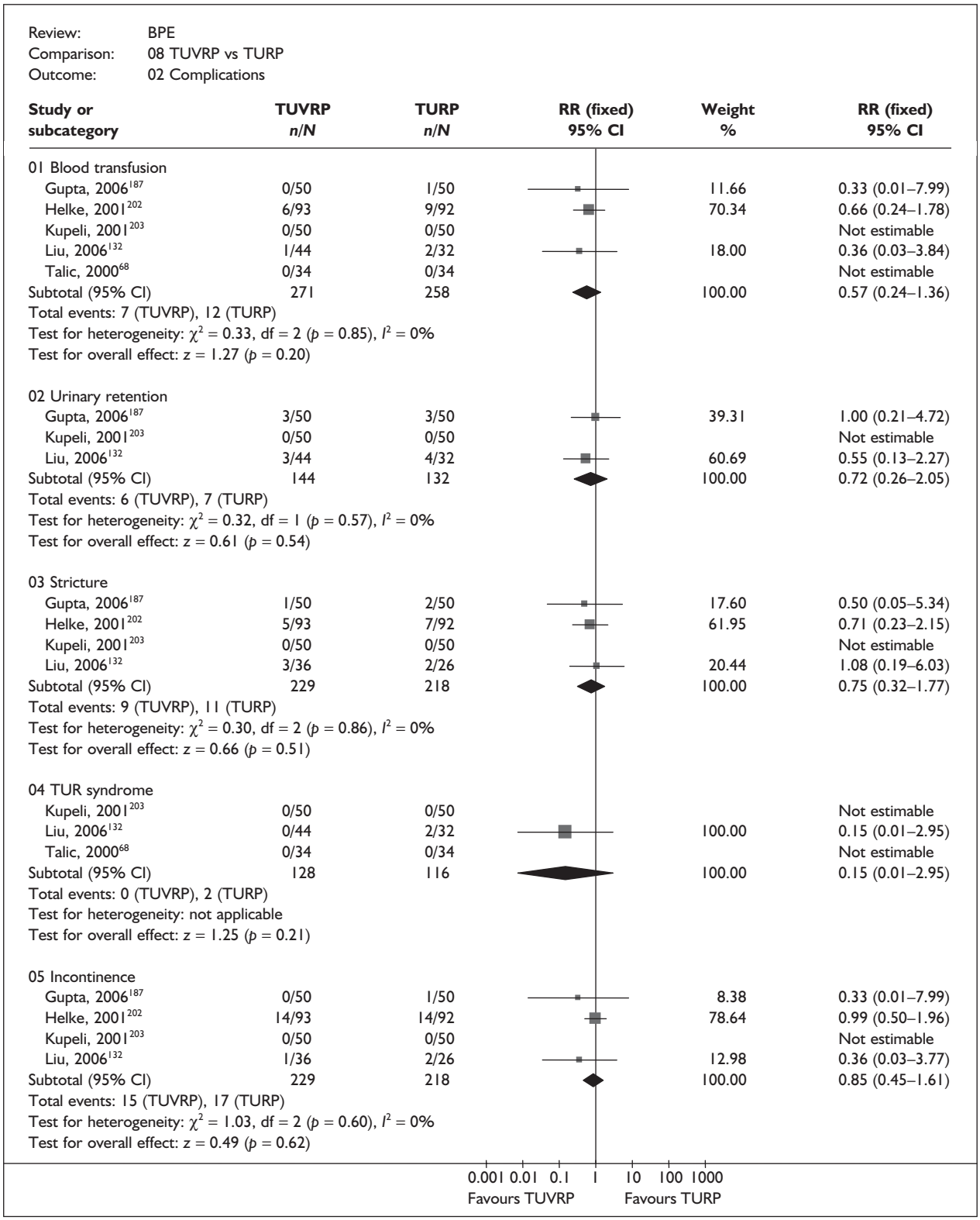


FIGURE 22 *Complications, TUVRP vs TURP.*

statistically significant (Appendix 9.8, comparison 08:06: WMD –1.91, 95% CI –8.80 to 5.07, $p = 0.59$).

Length of hospital stay

Only one study[132] provided information on length of hospital stay (Appendix 8.8, *Table 80*). The mean difference was less than a day (MD 0.41 days), favouring TUVRP. This was statistically significant (Appendix 9.8, comparison 08:07: 95% CI –0.54 to –0.28, $p < 0.001$).

Reoperation

Two studies[132,202] provided information on reoperation rates. Reoperation rates appeared to be higher in the TUVRP group (11.6%) than in the TURP group (5.9%). This difference, however, did not reach statistical significance (Appendix 9.8, comparison 08:02:13: RR 1.90, 95% CI 0.80–4.52, $p = 0.15$).

Summary and conclusions of the evidence for and against the intervention

This review considered data from over 500 randomised participants across five RCTs of generally moderate to low quality (and reporting). The data suggest that symptom scores, quality of life and peak urine flow rate do not differ between TUVRP and TURP. The incidence of blood transfusion, urinary retention, strictures, TUR syndrome and urinary incontinence was also similar in the two groups. The duration of operation and reoperation rates were also statistically similar in both groups; however, length of hospital stay was slightly shorter for TUVRP than it was for TURP.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 21*. These should be interpreted in view of the comments mentioned earlier in this chapter.

Bipolar transurethral resection of the prostate (B-TURP) versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 22*. Six RCTs[65,147,150,161,194,195] were eligible for this comparison, in which a total of 386 participants were randomised, 192 to B-TURP and 194 to conventional TURP.

Three trials took place in Turkey[161,194,195] and one each took place in India,[147] Korea[150] and Italy.[65] Five studies provided details of recruitment dates[147,150,161,194,195] with the earliest in 2001[194,195] and the latest in October 2004.[150]

All but one study[195] provided details of participants' IPSS/AUA scores at baseline, showing that 89 were severely symptomatic in each arm and 52 and 55 moderately symptomatic in the B-TURP and conventional TURP arms respectively.

Of the studies reporting prostate size,[65,147,161,194] all participants had large prostates.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.9. The results of the meta-analyses are given in Appendix 9.9. Note that in terms of long-term evaluation, only the longest follow-up is presented here.

Symptom scores

At 3 months

Data were available for only one[161] of five eligible trials. No differences in IPSS/AUA scores were observed between B-TURP and conventional TURP 3 months after surgery (*Figure 23*, comparison 09:01:01).

At 12 months

Of the three trials[65,161,194] providing information on IPSS/AUA scores, two[161,194] provided data that were suitable for meta-analysis. The improvement in symptoms in patients undergoing B-TURP was similar to that observed in conventional TURP patients (*Figure 23*; comparison 09:01:03: WMD 0.29, 95% CI –1.12 to 1.71, $p = 0.69$). This result is consistent with that observed in the study by de Sio and colleagues.[65]

Complications

The list of complications by study is detailed in Appendix 8.9, *Table 82*. Data describing nine complications were reported for one or more studies. The data were too few to provide precise estimates of differences and all confidence intervals were wide, such that clinically important differences could not be ruled out. Meta-analyses of the complications showed non-statistically significant differences between B-TURP and conventional TURP. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented

TABLE 21 *Summary of the clinical effect sizes from meta-analyses, TUVRP vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	1 (3)	0.30[a]	–0.63 to 1.23	0.53
12 months	2 (2)	–0.28[a]	–1.01 to 0.45	0.45
Longer term	1 (1)	0.60[a]	–1.09 to 2.29	0.49
Blood transfusion	5 (5)	0.57[b]	0.24–1.36	0.20
Urinary retention	3 (3)	0.72[b]	0.26–2.05	0.54
Stricture	4 (4)	0.75[b]	0.32–1.77	0.51
TUR syndrome	3 (3)	0.15[b]	0.01–2.95	0.21
Incontinence	4 (4)	0.85[b]	0.45–1.61	0.62
Quality of life				
3 months	1 (1)	0.20[a]	–0.09 to 0.49	0.18
Longer term	1 (1)	0.20[a]	–0.19 to 0.59	0.31
Q_{max}				
3 months	1 (2)	–0.90[a]	–1.84 to 0.04	0.06
12 months	2 (2)	0.10[a]	–0.41 to 0.61	0.70
Longer term	1 (1)	–1.60[a]	–3.50,0.30	0.10
Duration of operation	2 (2)	1.06[a]	–8.70 to 10.83	0.83
Length of hospital stay	1 (1)	–0.41[a]	–0.54 to –0.28	< 0.001
Reoperation	2 (2)	1.90[b]	0.80–4.52	0.15

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; TR, transurethral resection; TURP, transurethral resection of the prostate; TUVRP, transurethral vaporesection of the prostate.
a Weighted mean difference.
b Relative risk.

in this section (*Figure 24*). Results for other complications are presented in Appendix 9.9, comparison 09:02.

Quality of life

Three studies[65,147,161] reported quality of life of patients following surgery using the IPSS QoL (0–6) questionnaire, but only one study[161] presented data in a form that would allow quantitative synthesis. No statistically significant differences in quality of life were observed between B-TURP and conventional TURP at either the 3- or the 12-month follow-up (Appendix 9.9, comparison 09:07). This result is consistent with that reported by the studies that were not amenable to analysis.

Urodynamic outcomes

Data on peak urine flow rate, mean urine flow rate, residual volume and prostate size were reported to a varying extent across four studies[150,161,194,195] and are tabulated in Appendix 8.9, *Table 84*. Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 9.9, comparisons 09:03–09:06.

At 3 months

Two studies[161,195] provided details on peak urine flow rate for patients at 3 months after surgery. Across them, the average peak urine flow rate in the bipolar arm was not statistically significantly different from that observed in the conventional TURP arm (Appendix 9.9, comparison 09:03:01: WMD –0.98, 95% CI –2.25 to 0.29, $p = 0.13$).

At 12 months

Three studies[161,194,195] provided details on peak urine flow rate for patients at 12 months after surgery. There were no statistically significant differences between the two groups (Appendix 9.9, comparison 09:03:03: WMD 0.01, 95% CI –1.10 to 1.08, $p = 0.98$).

TABLE 22 *Summary of the baseline characteristics, B-TURP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
de Sio *et al.*, 2006[65]	B-TURP	35	59	24.2	7.1	80	52
	TURP	35	61	24.3	6.3	75	47
Kim *et al.*, 2006[150]	B-TURP	25	68	19.0	6.5	NR	53
	TURP	25	71	18.6	6.1	NR	52
Nuhoğlu *et al.*, 2006[194]	B-TURP	27	65	17.6	6.9	96	47
	TURP	30	65	17.3	7.3	88	49
Seckiner *et al.*, 2006[161]	B-TURP	24	61	24.1	8.5	88	49
	TURP	24	64	23.2	8.3	138	41
Singh *et al.*, 2005[147]	B-TURP	30	69	20.5	5.8	124	NR
	TURP	30	68	21.6	5.1	136	NR
Tefekli *et al.*, 2005[195]	B-TURP	51	69	NR	NR	NR	54
	TURP	50	69	NR	NR	NR	50

B-TURP, bipolar transurethral resection of the prostate; NR, not reported; TURP, transurethral resection of the prostate. Data given as mean values.
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association)

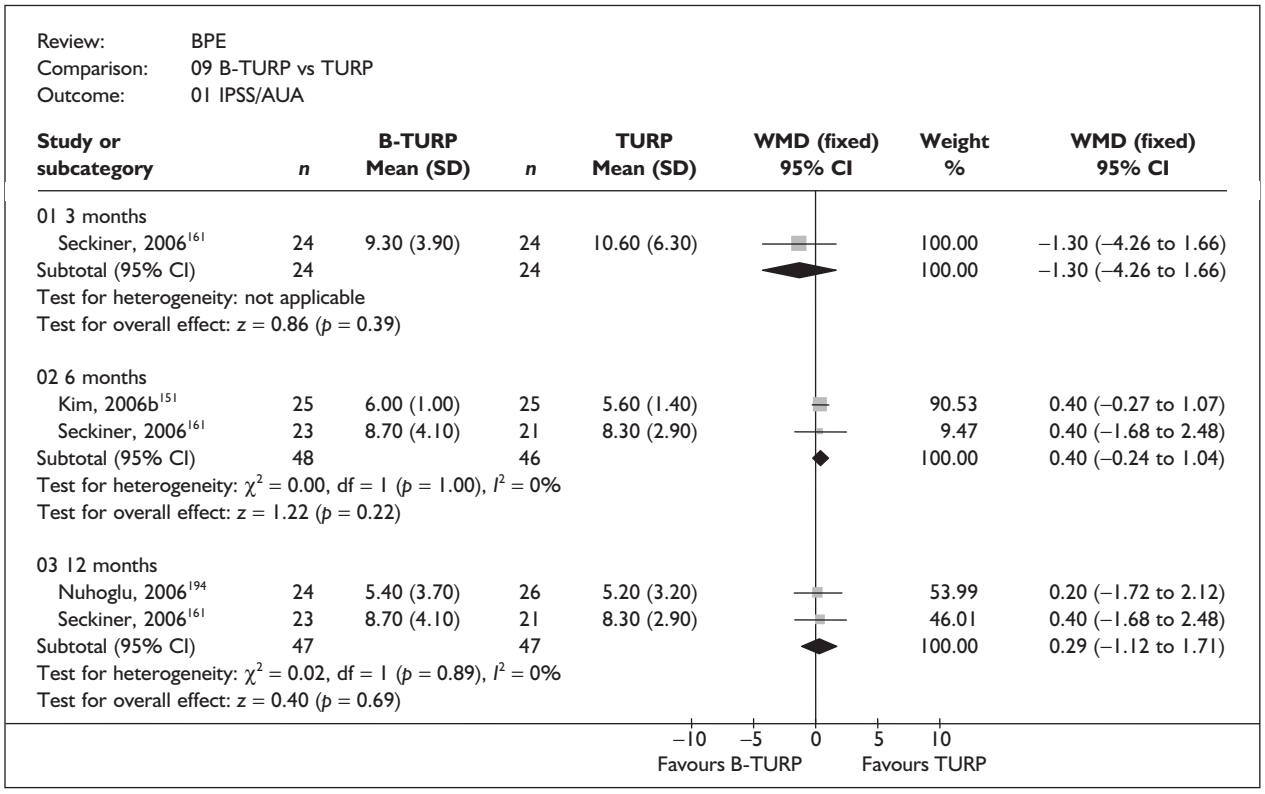


FIGURE 23 *Symptom scores, B-TURP vs TURP.*

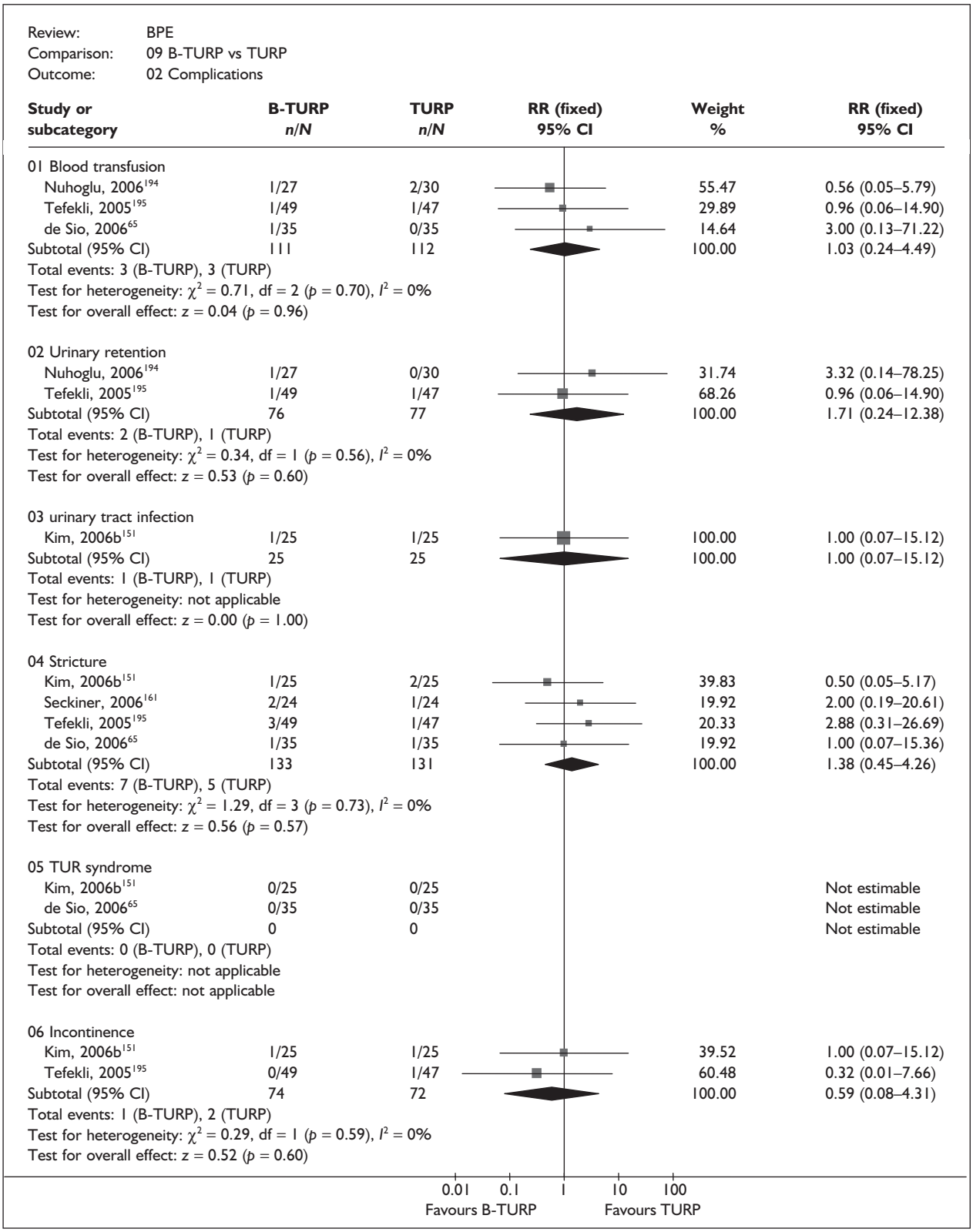


FIGURE 24 *Complications, B-TURP vs TURP.*

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.9, *Table 85*. Information on duration of operation and reoperations was identified to a varying extent across the eligible studies for this comparison.

Duration of operation

Five studies provided information on duration of operation, with the results being inconsistent (highly significant heterogeneity). Two[161,194] suggested no difference between the groups whereas, in another three,[65,150,195] a 3-, 5- and 17-minute difference in the mean length of operation, respectively, was observed, favouring B-TURP (Appendix 8.9, *Table 85*). Four studies provided data that were amenable to quantitative synthesis. Fitting a random-effects model resulted in a WMD of –4.56 minutes in favour of B-TURP. This result was not statistically significant (95% CI –15.36 to 6.23, $p = 0.41$).

Length of hospital stay

Evidence from two studies[65,150] suggests that the average length of stay following B-TURP was shorter than the average length of stay following TURP. The mean difference was –0.7 days (Appendix 8.9, *Table 85*; Appendix 9.9, comparison 09:10: 95% CI –01.37 to –0.03, $p = 0.04$).

Reoperation

Three studies[65,194,195] provided information on reoperation rates. No differences were observed between the two groups (Appendix 9.9, comparison 09:02:09: 3/111 versus 2/112, RR 1.46, 95% CI 0.25–8.57, $p = 0.67$). The time point of reoperation was unclear and the length of follow-up across studies ranged from 12 to 18 months.

Summary and conclusions of the evidence for and against the intervention

A total of 386 participants randomised to undergo B-TURP or conventional TURP across six RCTs of moderate to low quality were considered for this review. The data were too few to provide precise estimates for all of the outcomes considered and statistically significant differences could not be detected, with the exception of duration of operation, which bears significant heterogeneity and is of doubtful clinical or economic importance. A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 23*. These should be interpreted in view of the comments mentioned earlier in this chapter.

Bipolar transurethral vaporesection of the prostate (B-TUVRP) versus TURP

Characteristics of included studies

Only one RCT[155] making this comparison was identified in the searches (*Table 24*). This study, which was carried out in Hong Kong, allocated 29 men to undergo B-TUVRP and 31 to undergo TURP. Participants in both groups appeared to have moderate symptoms. No information was available to judge prostate size.

Assessment of effectiveness

This study reported outcomes on symptom scores, intraoperative and postoperative complications and quality of life. No urodynamic data were reported. These results are tabulated in Appendix 8.10, *Tables 86–89*.

Symptom scores

At 3 months

IPSS at 3 months were slightly better for B-TUVRP than for TURP. Patients in the B-TUVRP group showed a 54% improvement in mean scores from baseline compared with 39% in the TURP arm.

Complications

There was no difference in the incidence of urinary tract infections or clot retention after B-TUVRP and conventional TURP, with wide confidence intervals. There were no cases of TUR syndrome in either arm of the trial (*Table 25* and Appendix 9.10, comparison 10:01).

Quality of life

Quality of life in patients following B-TUVRP was comparable to that in the TURP group at the 3-month follow-up (Appendix 8.10, *Table 88*).[155]

Descriptors of care

There was no statistically significant difference between B-TUVRP and TURP in terms of duration of operation or length of hospital stay (Appendix 8.10, *Table 89*).

Transurethral vaporisation of the prostate (TUVP) versus TURP

Characteristics of included studies

The characteristics of the included studies are summarised in *Table 26*. Seventeen RCTs reported in 27 papers[55,57,128,129,138,140,142,156,158,162,193,196–201,262–271] randomised a total of 1449 participants.

TABLE 23 *Summary of the clinical effect sizes from meta-analyses, B-TURP vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	1 (3)	–1.30[a]	–4.26 to 1.66	0.39
12 months	2 (3)	0.29[a]	–1.12 to 1.71	0.69
Longer term	NR	NR	NR	NR
Blood transfusion	3 (3)	1.03[b]	0.24–4.49	0.96
Urinary retention	2 (2)	1.71[b]	0.24–12.38	0.60
Urinary tract infection	1 (1)	1.00[b]	0.07–15.12	1.00
Stricture	4 (4)	1.38[b]	0.45–4.26	0.33
TUR syndrome	2 (2)	NE	NE	NE
Incontinence	2 (2)	0.59[b]	0.08–4.31	0.60
Quality of life				
3 months	1 (3)	–0.30[a]	–0.92 to 0.32	0.35
12 months	1 (1)	–0.20[a]	–0.67 to 0.27	0.41
Longer term	NR	NR	NR	NR
Q_{max}				
3 months	2 (4)	0.98[a]	–0.29 to 2.25	0.13
12 months	3 (4)	0.01[a]	–1.08 to 1.10	0.98
Longer term	NR	NR	NR	NR
Duration of operation (minutes)	4 (5)	–4.56[a]	–15.36 to 6.23	0.41
Length of hospital stay (days)	1 (2)	–0.70[a]	–1.37 to –0.03	0.04
Reoperation	3 (3)	1.46[b]	0.25 to 8.57	0.67

B-TURP, bipolar transurethral resection of the prostate; IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; NE, not estimable; NR, not reported TUR, transurethral resection; TURP transurethral resection of the prostate.
a Weighted mean difference.
b Relative risk.

TABLE 24 *Summary of the baseline characteristics, B-TUVRP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Fung *et al.*, 2005[155]	B-TUVRP	29	72	15.8	NR	NR	NR
	TURP	31	73	19.4	NR	NR	NR

B-TUVRP, bipolar transurethral vaporesection of the prostate; NR, not reported; TURP transurethral resection of the prostate.
Data given as mean values.
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association).

TABLE 25 *Summary of the clinical effect sizes from meta-analyses, B-TUVRP vs TURP*

Outcome	Number of trials	Effect size	95% CI	*p*-value
Urinary tract infection	1	1.43	0.40–5.08	0.58
TUR syndrome	1	NE	NE	NE

B-TUVRP, bipolar transurethral vaporesection of the prostate; NE, not estimable; TUR, transurethral resection; TURP transurethral resection of the prostate.
a Mean difference.

Four studies took place in Turkey,[128,158,196,197] three in the UK,[57,129,162] three in the US,[55,140,199] and one each in Sweden,[142] Italy,[138] Japan,[156] the Netherlands,[193] Brazil,[198] Saudi Arabia[200] and China.[201] Eight studies gave details of the recruitment dates,[57,129,158,193,196,197,199,200] which ranged from 1995 to 2003.

All but two RCTs[55,196] reported participants' IPSS/AUA scores. The total number of participants who had severe symptoms of BPE and underwent TUVP was 487 (75%) compared with 408 (59%) with severe symptoms allocated to TURP. There were 160 (25%) participants with moderate symptoms allocated to TUVP and 284 (41%) with moderate symptoms allocated to TURP patients.

In the studies reporting prostate size, 322 (59%) and 225 (41%) participants allocated to TUVP had large and moderate-sized prostates, respectively, compared with 336 (58%) with large and 242 (42%) with moderate-sized prostates allocated to TURP.

Assessment of effectiveness

Tables giving a detailed description for all outcomes can be found in Appendix 8.11. The results of the meta-analyses are given in Appendix 9.11. Note that in terms of long-term evaluation, only the longest follow-up is presented here.

Symptom scores

At 3 months

Of the 18 eligible studies, 13 provided information on IPSS/AUA scores at 3 months after surgery (Appendix 8.11, *Table 90*). Meta-analysis of seven studies[55,57,138,156,162,199,200] showed no difference between TUVP and TURP in terms of symptom scores (*Figure 25*, comparison 11:01:01: WMD 0.09, 95% CI –0.42 to 0.61, $p = 0.72$). This result is consistent with the data from those trials that were not amenable to meta-analysis.

At 12 months

Eight studies provided information on the mean or median IPSS/AUA scores at 12 months (Appendix 8.11, *Table 90*). A meta-analysis involving five studies[55,129,138,193,200] reporting data that were suitable for synthesis again showed no statistically significant difference between the groups (*Figure 24*, comparison 11:01:03: WMD 0.34, 95% CI –0.19 to 0.86, $p = 0.21$). This result is consistent with the other three studies that were not amenable to meta-analysis.

Longer-term follow-up

Data from three studies[129,193,199] reporting IPSS scores at 5 years also showed little difference in symptom scores (*Figure 24*, comparison 11:01:07: WMD –0.32, 95% CI –1.95 to 1.31, $p = 0.70$).

Complications

Information about complications is detailed in Appendix 8.11, *Table 91*. Data describing 15 types of complications were reported to a varying extent across 15 studies. Results regarding blood transfusion, urinary retention, urinary tract infection, strictures, TUR syndrome and urinary incontinence are presented in this section (*Figure 26*). Results for other complications are presented in Appendix 9.11, comparisons 11:02 and 11:03. The results of these meta-analyses should be treated with caution as the length of follow-up of the RCTs varied and the confidence intervals were wide.

Blood transfusion

A total of 13 studies[55,57,128,129,138,140,156,158,162,193,196,197,199] reported blood transfusions. Meta-analysis suggested a lower rate of blood transfusion following TUVP than following TURP (*Figure 26*, comparison 11:02:01: 2/504 versus 29/537, RR 0.19, 95% CI 0.08–0.44, $p = 0.0001$).

TABLE 26 *Summary of the baseline characteristics, TUVP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Çetinkaya *et al.*, 1996[196]	TUVP	23	68	NR	NR	NR	48.4
	TURP	23	62	NR	NR	NR	48.8
Ekengren *et al.*, 2000[142]	TUVP	26	70	25[b]	NR	NR	NR
	TURP	28	71	22[b]	NR	NR	NR
Erdağı *et al.*, 1999[128]	TUVP	20	66	21.5	4.6	122.8	37.0
	TURP	20	64	20.6	5.1	68.0	32.5
Fowler *et al.*, 2005[57]	TUVP	115	70	20.7	10.1	181.0	54.3
	TURP	120	70	20.7	10.5	171.0	51.1
Gallucci *et al.*, 1998[138]	TUVP	70	NR	18.8	7.3	84.7	36.6
	TURP	80	NR	18.2	8.8	64.6	36.6
Gotoh *et al.*, 1999[156]	TUVP	23	70	19.6	7.3	56.7	56.7
	TURP	28	66	18.9	9.4	41.9	44.7
Hammadeh *et al.*, 2003[129]	TUVP	52	67	26.5	8.9	131.0	32.0
	TURP	52	70	26.6	8.6	101.0	27.0
Kaplan *et al.*, 1998[55]	TUVP	32	67	NR	NR	NR	NR
	TURP	32	73	NR	NR	NR	NR
Kupeli *et al.*, 1998[158]	TUVP	30	60	21.6	9.2	NR	51.7
	TURP	30	62	19.4	7.9	NR	48.9
Kupeli *et al.*, 1998[197]	TUVP	30	66	13.7	8.3	NR	41.6
	TURP	36	62	14.6	8.8	NR	43.6
Nathan and Wickham, 1996[162]	TUVP	20	65	21.9	10.2	132.0	53.5
	TURP	20	69	17.0	7.2	120.0	53.4
Netto *et al.*, 1999[198]	TUVP	40	67	19.6	7.9	73.0	46.9
	TURP	38	65	24.3	6.8	88.6	44.7
Nuhoğlu *et al.*, 2005[199]	TUVP	37	64	17.6	6.3	88.0	39.0
	TURP	40	65	17.3	5.9	95.0	39.0
Patel *et al.*, 1997[140]	TUVP	6	66	23.3	7.5	NR	64.6
	TURP	6	67	29.6	10.0	NR	54.0
Shokeir *et al.*, 1997[200]	TUVP	35	68	26.3	7.8	75.2	44.6
	TURP	35	68	25.1	6.9	77.1	48.8
Wang *et al.*, 2002[201]	TUVP	97	71	20	7.0	1231	NR
	TURP	109	72	20	7.0	120	NR
van Melick *et al.*, 2003[193]	TUVP	46	64	20.2	11.0	290.0	35.0
	TURP	50	66	16.8	11.0	350.0	37.0

NR, not reported; TURP transurethral resection of the prostate; TUVP, transurethral vaporisation of the prostate.
Data given as mean values (unless otherwise stated).
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association).
b Median.

Urinary retention

Pooling data from 11 studies[55,129,138,142,156,158,162,193,196,197,199] reporting this outcome showed a higher risk of urinary retention amongst those who underwent TUVP than amongst those who underwent TURP (*Figure 26*, comparison 11:02:02: 33/389 versus 15/419, RR 2.12, 95% CI 1.23–3.68, $p = 0.007$).

Urinary tract infection

Eight studies[55,128,129,138,156,162,193,197] provided details on the incidence of urinary tract infections after operation. A total of 21 (7.0%) urinary tract infections were reported amongst 298 participants allocated to TUVP compared with 33 (10.4%) amongst 318 participants allocated to TURP (*Figure 26*, comparison 11:02:03: RR 0.65, 95% CI 0.40–1.08, $p = 0.09$).

Stricture

Evidence from 11 studies showed no statistically significant difference between TUVP and TURP in terms of incidence of strictures or bladder neck contractures (*Figure 26*, comparison 11:02:04: 12/418 versus 14/446, RR 0.91, 95% CI 0.45–1.85, $p = 0.80$).

TUR syndrome

A total of three (0.9%) patients suffered a TUR syndrome following surgery amongst 314 randomised to TUVP as opposed to six (1.8%) amongst 329 patients randomised to TURP (*Figure 26*, comparison 11:02:05: RR 0.59, 95% CI 0.17–2.12, $p = 0.42$).

Urinary incontinence

Urinary incontinence was reported in nine studies (*Figure 26*). Urinary incontinence occurred less frequently in the TUVP arm than in the TURP arm. This difference was not statistically significant (*Figure 26*, comparison 11:02:06: 57/489 versus 64/533, RR 0.92, 95% CI 0.69–1.21, $p = 0.53$).

Quality of life

Five studies[57,129,142,162,193] reported quality of life of patients following surgery. In three studies, quality of life was assessed using the IPSS QoL (0–6) questionnaire. In the other two studies, authors did not provide further information on the measure used and later it was assumed that it was the IPSS QoL. One of the studies also assessed quality of life using the EQ-5D (using the UK tariff) and the SF-36 measures and the authors concluded that any change in general health-related quality of life resulting from their intervention was not detectable by either the EQ-5D or the SF-36 tools (the ranges and standard deviations were large).

There was no statistically significant difference in IPSS QoL at 3 or 12 months or for any longer-term follow-ups between TUVP and TURP following surgery (Appendix 9.11, comparison 11:10).

Urodynamic outcomes

Data on peak urine flow rate, mean urine flow rate, total voided volume, residual volume, detrusor pressure and prostate size were reported across 16 studies.[55,57,128,129,138,140,142,156,158,187,193,197–201] Only peak urine flow rate is presented in this section. Results for the other urodynamic outcomes are presented in Appendix 8.11, *Table 93* and Appendix 9.11, comparisons 11:04–11:09.

At 3 months

A total of 12 studies[55,57,128,129,138,140,156,158,187,193,199,200] provided details of peak urine flow rate at 3 months after surgery. In five studies[128,156,158,187,199] the average peak urine flow rate was higher in the TUVP group. A total of eight studies[55,57,138,156,158,193,199,200] presented data that were sufficiently similar to allow quantitative synthesis (Appendix 9.11, comparison 11:04:01). The WMD was 0.10 ml/s for TUVP versus TURP (95% CI –0.53 to 0.73, $p = 0.76$).

At 12 months

Nine studies[55,129,138,142,193,197,198,200,201] provided details of mean or median peak urine flow rate at 12 months after surgery. Five of the studies[55,142,197,198,201] reported lower rates in the TUVP group. Data from five trials[55,129,193,198,200] reporting data that were amenable to meta-analysis showed no statistically significant difference between TUVP and TURP (Appendix 9.11, comparison 11:04:03: WMD –0.11, 95% CI –0.97 to 0.74, $p = 0.80$).

Longer-term follow-up

Three studies[129,193,199] reported peak urine flow rate measurements 5 years after surgery. Meta-analysis of data from these trials showed no statistically significant difference between the two groups (Appendix 9.11, comparison 11:04:06: WMD 0.60, 95% CI –1.06 to 2.26, $p = 0.31$).

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.11, *Table 94*. Information on duration of operation, length of hospital stay and reoperation rates was identified to a varying extent across the 17 eligible studies for this comparison.

Review: BPE
Comparison: 11 TUVP vs TURP
Outcome: 01 IPSS/AUA

Study or subcategory	n	TUVP Mean (SD)	n	TURP Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
01 3 months							
Fowler, 2005[57]	105	11.80 (7.70)	110	9.80 (7.20)		6.66	2.00 (0.01–3.99)
Galluci, 1998[138]	70	5.50 (4.77)	80	5.52 (4.11)		12.87	–0.02 (–1.46 to 1.42)
Gotoh, 1999[156]	23	3.70 (2.40)	28	3.80 (2.30)		15.71	–0.10 (–1.40 to 1.20)
Kaplan, 1998[55]	32	9.20 (2.70)	32	8.60 (2.50)		16.31	0.60 (–0.67 to 1.87)
Nathan, 1996[162]	20	2.86 (2.80)	20	3.10 (2.30)		10.51	–0.24 (–1.83 to 1.35)
Nuhoglu, 2005[199]	35	4.70 (3.10)	38	4.80 (4.20)		9.34	–0.10 (–1.78 to 1.58)
Shokeir, 1997[200]	35	4.50 (1.90)	35	4.80 (2.20)		28.59	–0.30 (–1.26 to 0.66)
Subtotal (95% CI)	320		343			100.00	0.09 (–0.42 to 0.61)
Test for heterogeneity: $\chi^2 = 5.09$, df = 6 ($p = 0.53$), $I^2 = 0\%$							
Test for overall effect: $z = 0.35$ ($p = 0.72$)							
02 6 months							
Fowler, 2005[57]	106	8.50 (7.40)	108	6.90 (5.50)		6.66	1.60 (–0.15 to 3.35)
Galluci, 1998[138]	70	4.94 (4.68)	80	3.77 (3.30)		11.83	1.17 (–0.14 to 2.48)
Kaplan, 1998[55]	32	7.40 (2.90)	32	7.90 (3.10)		9.43	–0.50 (–1.97 to 0.97)
van Melick, 2003a[193]	33	3.80 (2.70)	37	3.20 (2.70)		12.70	0.60 (–0.67 to 1.87)
Shokeir, 1997[200]	35	4.60 (1.20)	35	4.50 (1.30)		59.38	0.10 (–0.49 to 0.69)
Subtotal (95% CI)	276		292			100.00	0.33 (–0.12 to 0.79)
Test for heterogeneity: $\chi^2 = 5.59$, df = 4 ($p = 0.23$), $I^2 = 28.4\%$							
Test for overall effect: $z = 1.45$ ($p = 0.15$)							
03 12 months							
Galluci, 1998[138]	70	4.04 (4.26)	80	3.52 (3.04)		19.24	0.52 (–0.68 to 1.72)
Hammadeh, 2003[129]	51	4.40 (3.80)	51	5.90 (5.20)		8.87	–1.50 (–3.27 to 0.27)
Kaplan, 1998[55]	30	6.60 (2.40)	31	6.10 (1.90)		23.38	0.50 (–0.59 to 1.59)
van Melick, 2003a[193]	34	4.80 (4.90)	41	4.10 (4.80)		5.69	0.70 (–1.51 to 2.91)
Shokeir, 1997[200]	25	5.20 (1.40)	25	4.70 (1.50)		42.82	0.50 (–0.30 to 1.30)
Subtotal (95% CI)	210		228			100.00	0.34 (–0.19 to 0.86)
Test for heterogeneity: $\chi^2 = 4.59$, df = 4 ($p = 0.33$), $I^2 = 12.8\%$							
Test for overall effect: $z = 1.26$ ($p = 0.21$)							
04 18 months							
Gotoh, 1999[156]	28	3.83 (4.62)	27	8.68 (2.30)		100.00	–4.85 (–6.77 to –2.93)
Subtotal (95% CI)	28		27			100.00	–4.85 (–6.77 to –2.93)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 4.95$ ($P < 0.00001$)							
05 2 years							
Fowler, 2005[57]	90	8.60 (7.20)	77	7.50 (5.80)		37.74	1.10 (–0.87 to 3.07)
Hammadeh, 2003[129]	47	4.30 (3.50)	47	6.30 (4.30)		58.45	–2.00 (–3.59 to –0.41)
van Melick, 2003a[193]	12	8.40 (8.70)	15	5.80 (7.50)		3.80	2.60 (–3.62 to 8.82)
Subtotal (95% CI)	149		139			100.00	–0.66 (–1.87 to 0.56)
Test for heterogeneity: $\chi^2 = 6.86$, df = 2 ($p = 0.03$), $I^2 = 70.8\%$							
Test for overall effect: $z = 1.06$ ($p = 0.29$)							
06 3 years							
Hammadeh, 2003[129]	40	4.10 (3.30)	40	7.10 (6.20)		100.00	–3.00 (–5.18 to –0.82)
Subtotal (95% CI)	40		40			100.00	–3.00 (–5.18 to –0.82)
Test for heterogeneity: not applicable							
Test for overall effect: $z = 2.70$ ($p = 0.007$)							
07 5 years							
Hammadeh, 2003[129]	27	5.90 (6.30)	27	8.60 (7.10)		20.71	–2.70 (–6.28 to 0.88)
van Melick, 2003a[193]	12	7.00 (5.60)	15	7.30 (7.10)		11.57	–0.30 (–5.09 to 4.49)
Nuhoglu, 2005[199]	21	6.50 (3.20)	23	6.10 (3.50)		67.73	0.40 (–1.58 to 2.38)
Subtotal (95% CI)	60		65			100.00	–0.32 (–1.95 to 1.31)
Test for heterogeneity: $\chi^2 = 2.21$, df = 2 ($p = 0.33$), $I^2 = 9.3\%$							
Test for overall effect: $z = 0.39$ ($p = 0.70$)							

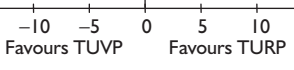


FIGURE 25 *Symptom scores, TUVP vs TURP.*

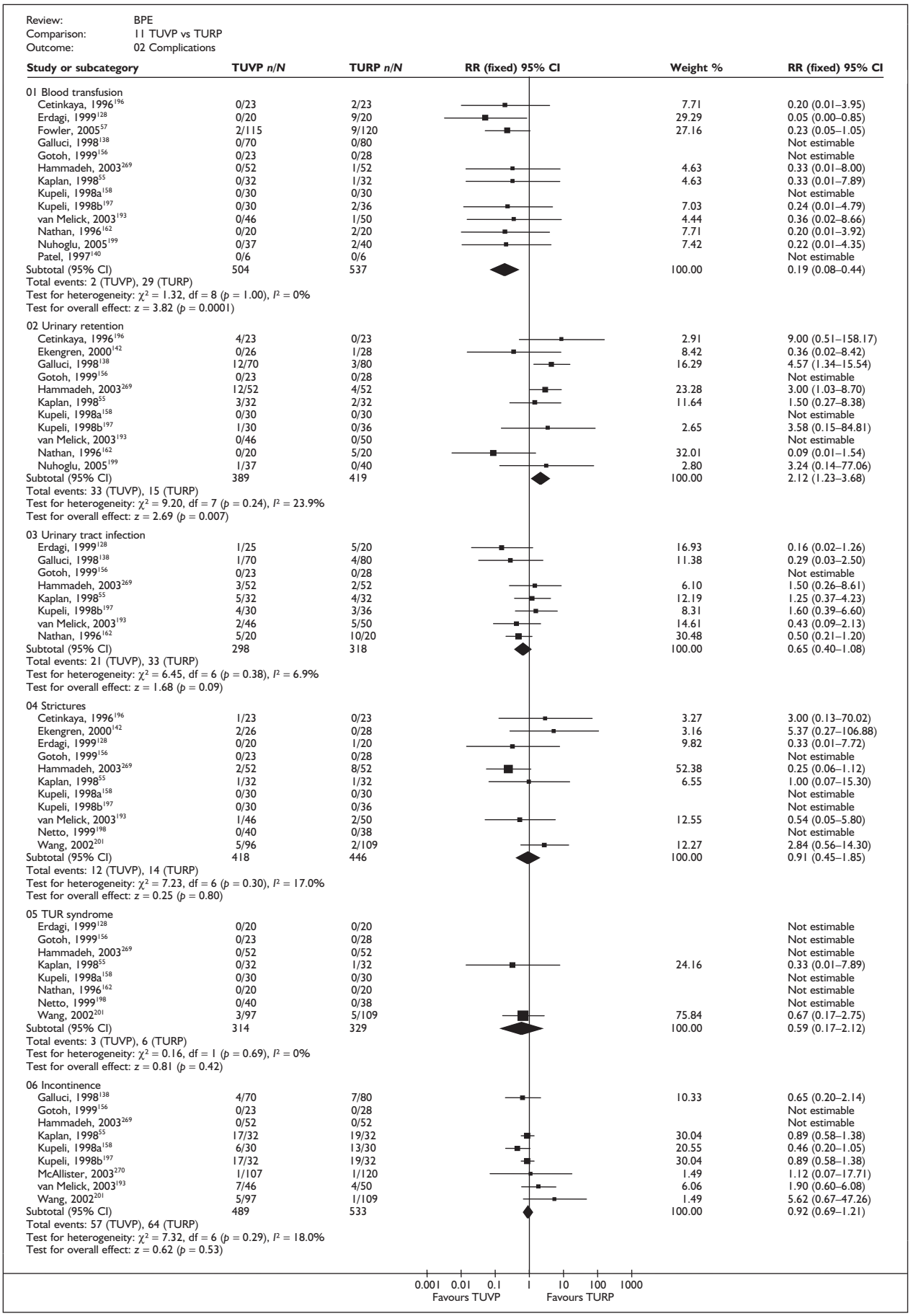


FIGURE 26 *Complications, TUVP vs TURP.*

Duration of operation

A total of 14 studies[55,57,129,140,142,156,158,162,193,196,198–201] reported duration of operation (Appendix 8.11, *Table 94*). In half of the studies[55,57,129,158,162,199,200] this was longer in the TUVP group whereas in the other half[140,142,156,193,196,198,201] it was shorter in the TUVP group. Eight studies presented data in a form sufficiently similar to allow quantitative synthesis (Appendix 9.11, comparison 11:11). The WMD was –1.62 minutes, favouring TUVP, although this was not statistically significant (95% CI –12.23 to 8.99, $p = 0.76$).

Length of hospital stay

Ten studies[55,57,129,138,140,162,193,197,198,200] provided information on length of hospital stay (Appendix 8.11, *Table 94*). In all but two studies[57,193] length of hospital stay was reported to be shorter for TUVP. In two studies there were no differences. Eight RCTs[55,57,129,138,193,197,198,200] reported data that were suitable for synthesis. Across them, the average length of stay was 1.00 day less following TUVP (Appendix 9.11, comparison 11:12: WMD –1.00, 95% CI –1.25 to –0.75, $p < 0.001$).

Reoperation

Only seven studies[129,142,162,193,197,199,270] out of a possible 17 reported reoperation rates. The risk of having a reoperation following TUVP was no different from that following TURP. However, the confidence intervals were wide enough for clinically important differences to exist between the two groups (Appendix 9.11, comparison 11:03:15: 14/326 versus 14/346, RR 1.04, 95% CI 0.53–2.07, $p = 0.90$).

Summary and conclusions of the evidence for and against the intervention

This review considered data from 1449 randomised participants across 17 RCTs of moderate to low quality. The data suggest that the rates of blood transfusion and urinary tract infection are lower and the rate of urinary retention is higher after TUVP than after TURP. The length of hospital stay for TUVP was shorter in the trials. There were no statistically significant differences in IPSS/AUA symptom scores, quality of life and peak urine flow rate at 3 or 12 months or at any longer-term follow-up between TUVP and TURP. The incidence of complications such as strictures, TUR syndrome and urinary incontinence was similar. Duration of operation and reoperation rates also did not appear to differ between the two groups.

There was evidence of high statistical heterogeneity in the results for peak urine flow rate, quality of life, duration of operation and length of hospital stay. There was no consistency in the direction of effect and clinically important differences could not be ruled out. Much of the variation might be due to differences in participants' characteristics or the ways in which the technologies were used. In addition, differences in the specific aims and objectives of the studies might have led to important differences in their inclusion criteria. In the case of duration of operation, the variation may be explained by differences in operator experience and baseline prostate size, which can be considered as a proxy for duration of operation.

Clinical effect size

A summary of the clinical effect sizes for all outcomes derived from the meta-analyses for which data were available is given in *Table 27*.

Bipolar transurethral vaporisation of the prostate (B-TUVP) versus TURP

Characteristics of included studies

Only two RCTs making this comparison were identified by the searches (*Table 28*).[70,137,272] One study took place in Australia[137,272] and the other in the UK.[70] A total of 111 men were allocated to undergo B-TUVP and 100 to undergo TURP. Participants in the bipolar group appeared to have severe symptoms whereas 21 (21%) of those in the TURP group had moderate symptoms and 79 (79%) had severe symptoms preoperatively. Participants in the bipolar group had moderate-sized prostates whereas those in the TURP group had large prostates.

Assessment of effectiveness

Symptom scores

Data reported in the study by Dunsmuir and colleagues[137,272] showed better improvement in mean AUA scores at 3 months for bipolar TUVP than for TURP (Appendix 8.12, *Table 95*). In contrast, Hon and colleagues[70] did not find any statistically significant difference between the two groups at 9 months following surgery (Appendix 9.12, comparison 12:01:01: MD 0.80, 95% CI –1.23 to 2.83, $p = 0.44$).

Complications

Four types of complication were identified, with no statistically significant differences between the groups (Appendix 9.12, comparison 12:02).

TABLE 27 *Summary of the clinical effect size from meta-analyses, TUVP vs TURP*

Outcome	Number of trials MA (total)	Effect size	95% CI	*p*-value
IPSS/AUA score				
3 months	7 (13)	0.09[a]	–0.42 to 0.61	0.72
12 months	5 (8)	0.34[a]	–0.19 to 0.86	0.21
Longer term	3 (3)	–0.32[a]	–1.95 to 1.31	0.70
Blood transfusion	13 (13)	0.19[b]	0.08–0.44	< 0.001
Urinary retention	11 (11)	2.12[b]	1.23–3.68	0.007
Urinary tract infection	8 (8)	0.65[b]	0.40–1.08	0.09
Stricture	11 (11)	0.91[b]	0.45–1.85	0.80
TUR syndrome	8 (8)	0.59[b]	0.17–2.12	0.42
Incontinence	9 (9)	0.92[b]	0.69–1.21	0.53
Quality of life				
3 months	1 (2)	0.30[a]	–0.18 to 0.78	0.22
12 months	2 (3)	0.47[a]	–0.23 to 0.32	0.73
Longer term	1 (1)	–0.60[a]	–1.30 to 0.10	0.09
Q_{max}				
3 months	8 (12)	0.10[a]	–0.53 to 0.73	0.78
12 months	5 (10)	–0.11[a]	–0.97 to 0.74	0.80
Longer term	3 (3)	0.60[a]	–1.06 to 2.26	0.48
Duration of operation	8 (14)	–1.62[a]	–12.23 to 8.99	0.76
Length of hospital stay	8 (11)	–1.00[a]	–1.25 to –0.75	< 0.001
Reoperation	7 (7)	1.04[b]	0.53–2.07	0.90

IPSS/AUA, International Prostate Symptom Score/American Urological Association; MA, meta-analysed; TUR, transurethral resection of the prostate; TUVP, transurethral vaporisation of the prostate.
a Weighted mean difference.
b Relative risk.

Quality of life

Both studies reported quality of life of patients following surgery. The IPSS QoL scale was used in one study[70] and the AUA QoL in the other.[137,272] AUA QoL was taken from section C of the AUA7 system. It comprises five questions to give a maximum score of 19. No statistically significant differences were observed between the two groups at 3, 9 and 12 months following surgery (Appendix 8.12, *Table 97*; Appendix 9.12, comparison 12:04:01).

Urodynamic outcomes

Data on peak urine flow rate, mean flow rate and residual volume were reported across the two studies. Results for these outcomes are presented in Appendix 8.12, *Table 98* and Appendix 9.12, comparisons 12:05–12:07. No statistically significant differences were identified between the two groups.

Descriptors of care

Data describing descriptors of care are tabulated in Appendix 8.12, *Table 99*. Information on duration of operation, length of hospital stay and reoperation rates were identified across the two eligible studies for this comparison.

Duration of operation

Duration of operation was found to be longer in the B-TUVP arm than in the TURP arm in the two studies reporting this outcome (Appendix 8.12, *Table 99*; Appendix 9.12, comparison 12:08).

TABLE 28 *Summary of the baseline characteristics, B-TUVP vs TURP*

Study	Comparators	Number of participants	Age (years)	Symptom score[a]	Q_{max} (ml/s)	Residual volume (ml)	Prostate size (ml)
Dunsmuir *et al.*, 2003[137,272]	B-TUVP	30	63	24	9.6	112	39
	TURP	21	60	17	10.4	96	42
Hon *et al.*, 2006[70]	B-TUVP	81	66	21	12	147	38
	TURP	79	68	21	12	182	40

B-TUVP, bipolar transurethral vaporisation of the prostate; TURP, transurethral resection of the prostate.
Data given as mean values.
a Symptom scores given as IPSS/AUA (International Prostate Symptom Score/American Urological Association).

Length of hospital stay

Both studies reported this outcome (Appendix 8.12, *Table 99*). In one study[137,272] length of hospital stay in the B-TUVP arm was no different from that observed in the TURP arm ($p = 0.78$). The other study reported a higher mean length of hospital stay in the B-TUVP arm than in the TURP arm (Appendix 9.12, comparison 12:09: MD –0.40, 95% CI –0.71 to –0.01, $p = 0.01$).

Reoperation

Evidence based on one study showed that there was no statistically significant difference in reoperation rates between the two arms (Appendix 9.12, comparison 12:02:05: 1/81 versus 2/79, RR 0.49, 95% CI 0.05–5.27, $p = 0.55$).

Chapter 9

Most promising intervention(s) for benign prostatic enlargement

Because of the lack of RCTs comparing minimally invasive interventions with ablative methods other than TURP, a narrative review investigating trends across the interventions was performed to identify the most promising minimally invasive and ablative methods. For all comparisons considered, symptom scores are reported on the same forest plot (*Figures 27* and *28*). Plots for other outcomes can be seen in Appendix 9.14. These forest plots can be used to illustrate the differences between interventions.

There does not appear to be a clear winner in terms of which intervention is the most promising to treat BPE. Some interventions perform better when assessed in terms of one outcome than others. Interpretation is difficult because of the paucity of data and the multitude of comparators. However, in summary, there seems to be little evidence that any treatment is more effective than TURP in terms of resolution of symptoms of BPE. What evidence there is relates to improvement in peak urine flow rate (laser resection better) with doubtful translation to clinically significant benefit. Several procedures appear to perform better than TURP, at least in terms of one measure of complications. The performance of the different interventions relative to TURP is detailed in *Table 29*.

Given that the results indicate that there are trade-offs between the outcomes provided by different treatments, patient preference becomes more important. However, these choices might be informed by the synthesis of the different clinical outcomes into a single measure, as performed in Chapter 10.

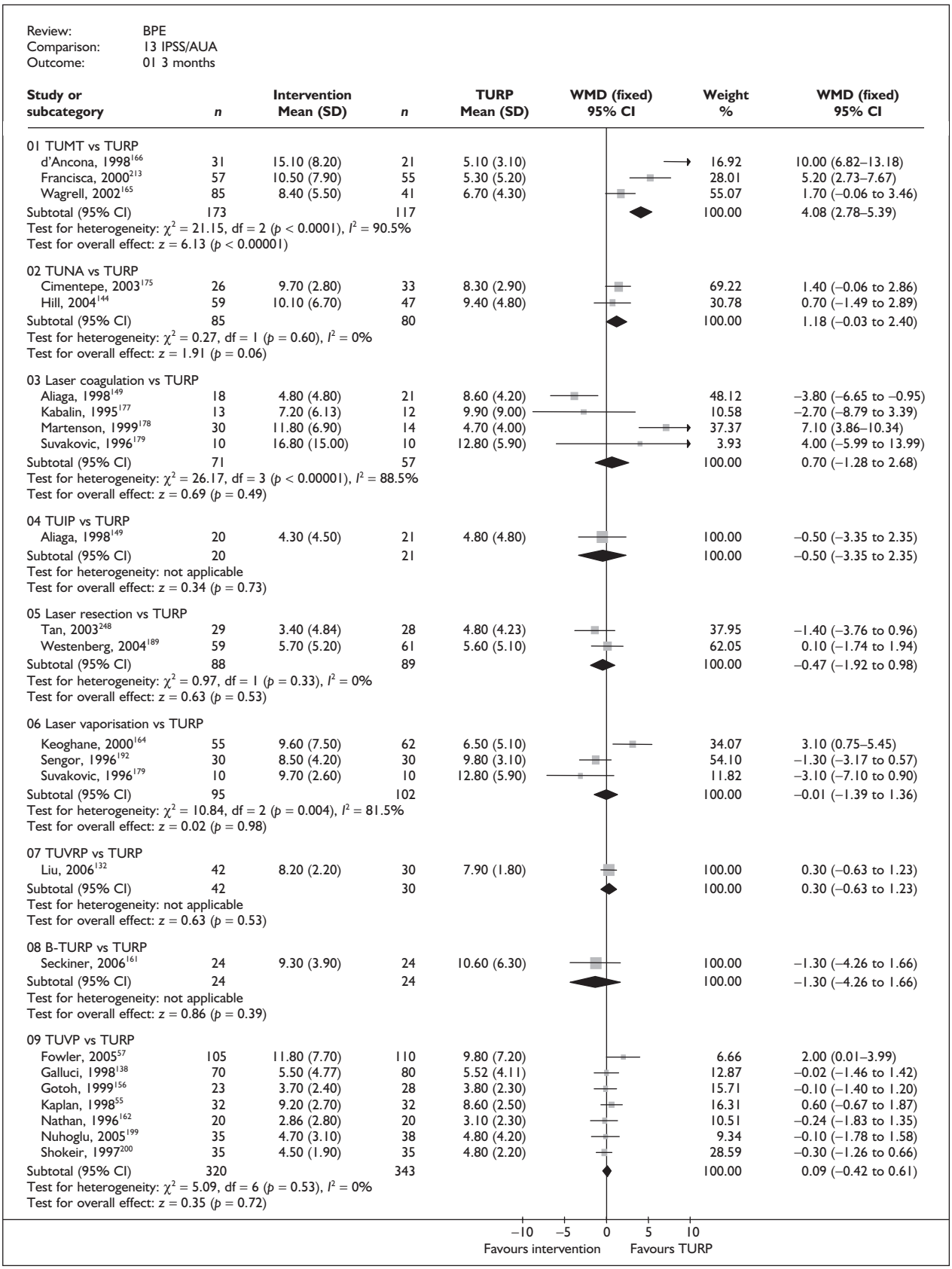


FIGURE 27 *IPSS/AUA scores by comparison at 3 months.*

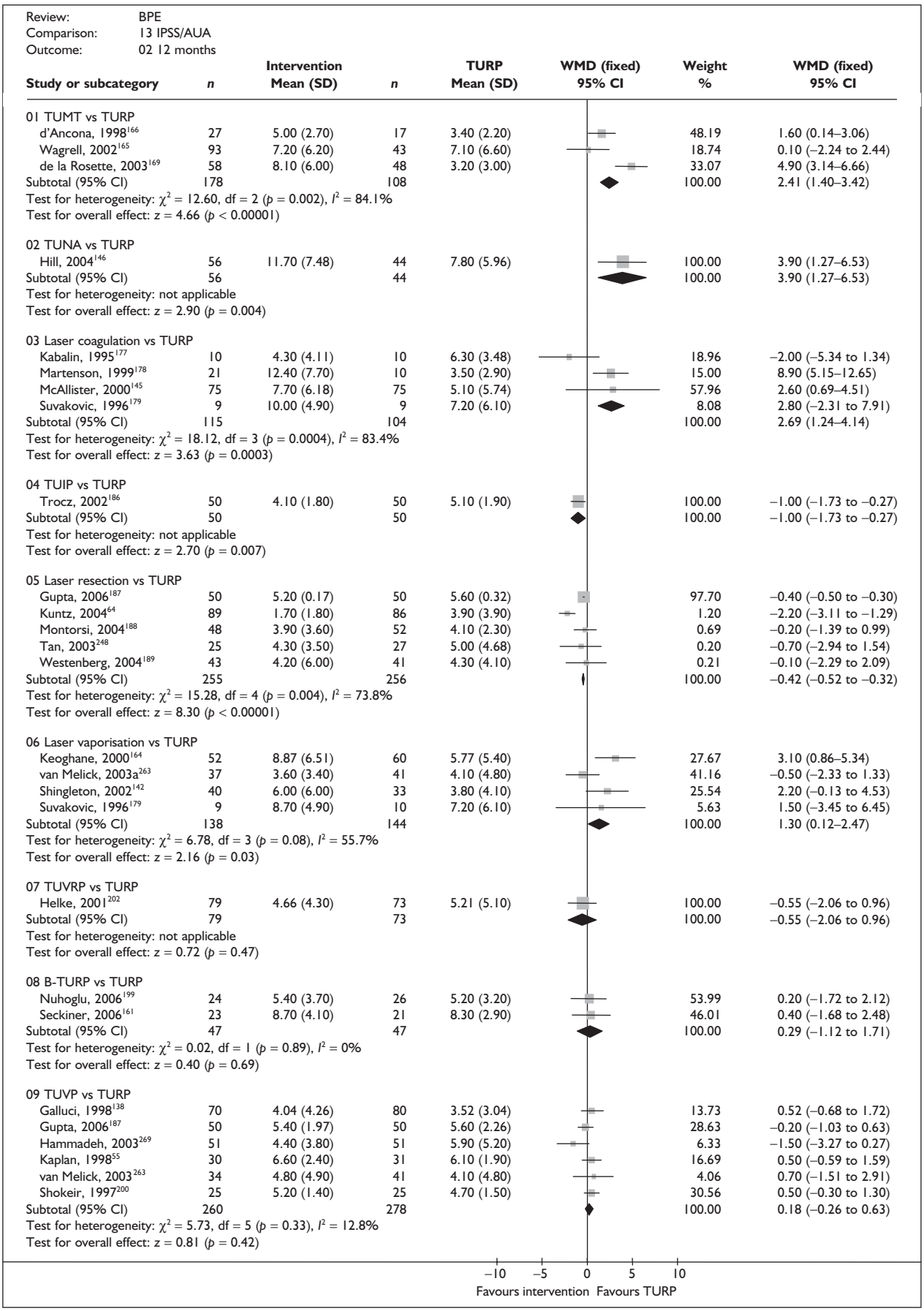


FIGURE 28 *IPSS/AUA scores by comparison at 12 months.*

TABLE 29 *Balance sheet detailing performance of the different interventions relative to TURP*

Outcome	Relative to TURP												
	TUMT	**TUNA**	**Stents**	**TEAP**	**Laser coagulation**	**TUIP**	**HoLEP**	**Laser vaporisation**	**TUVRP**	**B-TURP**	**B-TUVRP**	**TUVP**	**B-TUVP**
IPSS, 12 months	W	W	U	U	W	U	S	W	S	U	U	S	U
Blood transfusion	U	B	U	U	B	B	B	B	S	S	U	B	U
Urinary retention	U	U	U	U	W	U	S	W	U	S	U	W	U
Urinary tract infection	S	S	U	U	W	S	S	S	U	S	U	B	U
Stricture	B	B	U	U	B	S	S	B	S	S	U	S	U
TUR syndrome	U	U	U	U	U	U	U	U	U	U	U	S	U
Incontinence	U	B	U	U	B	S	S	W	S	U	U	S	U
Quality of life, 12 months	W	S	U	U	W	U	U	S	S	S	U	S	U
Q_{max}, 12 months	W	W	U	U	W	W	B	U	U	S	U	S	U
Duration of operation	U	W	U	U	B	B	W	S	S	S	U	S	U
Length of stay	B	U	U	U	B	B	B	B	U	B	U	B	U
Reoperation	U	W	U	U	W	W	S	U	S	S	U	S	U

B-TURP, bipolar transurethral vaporisation of the prostate; B-TUVP, bipolar transurethral resection of the prostate; B-TUVRP, bipolar transurethral vaporisation of the prostate; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; TEAP, transurethral ethanol ablation of the prostate; TUIP, transurethral incision of the prostate; TUMT, transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TUR, transurethral resection; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate; TUVRP, transurethral vaporesection of the prostate.
B, intervention performs better than TURP for the outcome; S, intervention performs the same as TURP for the outcome; U, estimate is too imprecise or there is lack of evidence; W, intervention performs worse than TURP for the outcome.

Chapter 10
Economic analysis

The economic perspective was that of the English NHS and, in the base case, the time horizon was 10 years, which was chosen because it was believed a priori that this would be sufficient to show the difference between technologies. A discount rate of 3.5% for costs and benefits was used in the base case, but this was varied in sensitivity analysis. The price year was 2006 and the currency was UK pounds sterling.

Multiple versus single cohort analysis

A time horizon of 'until death' was planned for a sensitivity analysis. However, the need to incorporate capital costs (e.g. for HoLEP) led to a change in model structure from one that is 'individual based' [i.e. estimating the expected cost and quality-adjusted life-years (QALYs) per individual] to one that is 'population based'. The standard individual-based model structure is identical to averaging across a cohort of identical individuals all starting treatment at the same time. The approach used in this analysis allowed for new individuals to enter over a time period, which we assumed was the approximate lifetime of the technologies of 10 years. This is equivalent to having multiple versus single cohort analysis. This means that there is a 'mixing' of individuals over time such that at 1-year post technology change there will be equal numbers of those receiving their first treatment (0 years post treatment) and those who are 1-year post first treatment. After 10 years there will thus be equal numbers from year 0 to year 10 post treatment. This allows for the incorporation of capital equipment costs over the time horizon as required for strategies in which equipment is not used as the first-line treatment but rather to manage subsequent failure of treatment or relapse. For example, in the strategy TUVP/HoLEP, HoLEP is never used as the first-line treatment and it is clear that, over time, as more new individuals are treated, the amount of HoLEP equipment required will increase.

Such a model involves greater complexity in that, as described below, the model must 'keep track' of time post technology introduction (for the whole population) as well as time post first treatment (for the individual, including age-dependent mortality). However, this approach allows the simulation of the purchasing of new equipment as required over the time horizon and produces a more accurate estimation of costs and effectiveness and thus cost-effectiveness.

The rest of this chapter is subdivided in the same way as in the review of economic evaluation reported in Chapter 4 except that the section on sensitivity analysis deals only with the probabilistic analysis. As already explained, deterministic sensitivity analysis is reserved for testing the effect of parameter variability or model structure uncertainty and is therefore dealt with under the subheadings below.

Population

The population is men with a specified mean start age with a diagnosis of BPE (no other size criteria), presence of LUTS (with a measure of IPSS > 7), no complications and TURP indicated. This implies that medical treatment is either contraindicated or has failed. In the base-case analysis the mean start age was 70. This value was chosen because it lies approximately in the middle of the current range of age at treatment. In the sensitivity analysis the mean start age has been varied between 50 and 90 because this represents approximate ranges for the defined population.

The technologies to compare

The strategies chosen were those that the clinical experts believed to be clinically appropriate and were designed to adequately capture events that were likely to incur costs and health changes over the 10-year time horizon of the model. The strategies were formulated over the course of several meetings of clinicians involved in the study supplemented by discussion with the health economist and with additional input from other urologist colleagues to resolve differences in opinion. A time horizon of 10 years was chosen because it was believed a priori that this would

be sufficient to show the differences between technologies.

The problem with using strategies is that the comparison of each possible sequence of treatments is costly in terms of building and estimating the model and, until the model is completed, it cannot be used to eliminate any sequences. However, the guiding principle at each step of the research process is the perceived value of information analysis, based on the current evidence. Before undertaking any calculation of value of information based on the model itself, judgement is required as to whether a particular sequence is feasible for the given setting and is sufficiently important to warrant the additional research cost of adding that sequence. Therefore, treatment sequences were reduced according to a set of clinical rules regarding treatments in the minimally invasive (M), TURP (T) and other tissue ablative (A) categories, and:

1. Always proceed from less to more invasive.
2. Never repeat one of the other tissue ablative procedures.
3. Repeat a minimally invasive procedure no more than once.
4. Repeat TURP only once and only after performing a pressure test.
5. Never change to another treatment from the same category.

The basis for (1) is the belief that if a more invasive treatment is ineffective then the less invasive one will also be ineffective. The second assumption is tantamount to saying that any change due to tissue ablative treatments renders the prostate 'immune' to further benefit from this class of treatments. The third assumption is based on the belief that additional structural change to the prostate is extremely unlikely to occur given two previous attempts. The fourth is based on standard practice within the UK. The fifth is based on the belief that if one procedure in a category has failed then another from the same category is unlikely to be more successful than repeating the same procedure and that no more than one treatment from the same category is likely to be available in any given institution.

The strategies compared in the DAM were:

1. One treatment only: M, A, T.
2. Two treatments: MM, MA, MT, AT, TT.
3. Three treatments: MMA, MMT, MAT, MTT.
4. Four treatments: MMAT, MMTT, MATT.
5. Five treatments: MMATT.

Out of all possible treatments in each of the categories, a representative was chosen based on the one most likely to be used in the UK: TUMT and laser coagulation in the minimally invasive category; and TUVP in the tissue ablative category. Two further treatments were added: laser resection, as exemplified by HoLEP; and laser vaporisation, as exemplified by KTP. HoLEP was treated as a TURP substitute but without the possibility that it could be repeated as it was believed that it removes so much tissue that there can be no subsequent treatment. KTP was treated as a substitute for TUVP.

The epidemiology: model structure

A Markov model was used in which health states and order of transitions were determined a priori according to a logical sequence of events (e.g. treatment cannot follow death) and expert clinical judgement (e.g. permanent urinary incontinence contraindicates further treatment). The cycle length was set at 3 months. This was based on the advice by the clinical expert group that there was unlikely to be any difference between treatments over a shorter time period. Given the length of follow-up of 10 years this meant that costs and effects were estimated over 40 cycles. As described above, as well as estimating the consequences (cost and QALYs) accruing to each individual over time, these consequences were summed over a population over 10 years. This was operationalised by creating another 'state' from which new individuals could enter the model in each cycle. For simplicity this state is not included in the diagram below. The number of new individuals was assumed to be 25,000 per year, which is approximately the number of first TURP procedures per year in the UK. This was estimated from the NHS reference costs, 2005–6,[45] assuming that approximately 5% of all TURPs in a year are reoperations.

Figure 29 shows a generic component of the Markov model, which represents the care pathway shown in *Figure 1*, in which each box corresponds to a health state. Given survival (i.e. no death) there are two main dimensions of outcome (incontinence or not and remission or not), which, being independent, imply four possible health state transitions following treatment. The state of death, which is not shown, is an absorbing state in that it cannot be left and it can also be entered from any

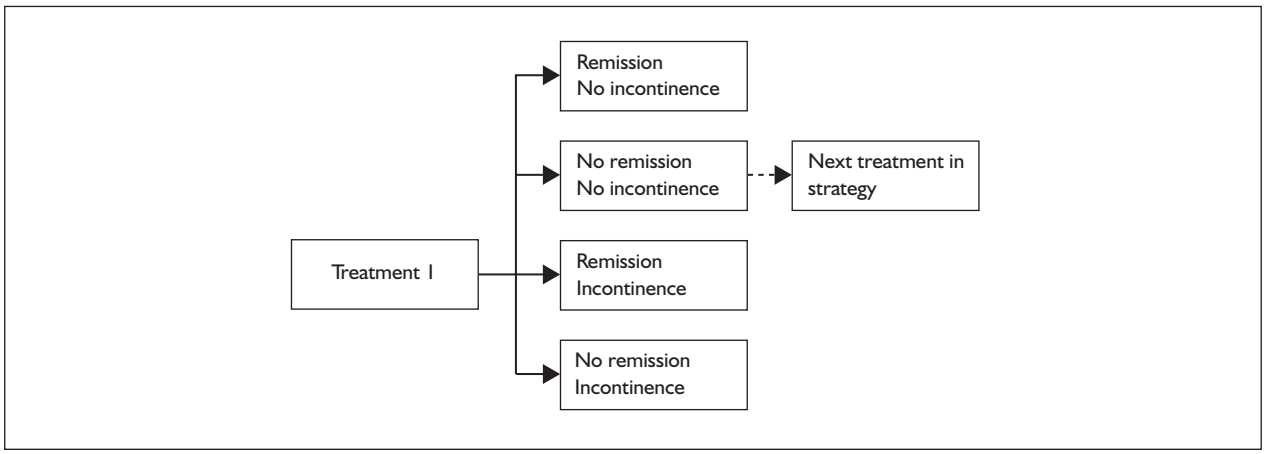


FIGURE 29 *Schematic of Markov model component.*

of the other states. In keeping with the argument presented in Chapter 4, the only long-term complication that needed to be included in the DAM was incontinence. The states of 'no remission' (whether with incontinence or not) are entered with the probability of failure for that particular treatment. This defines failure as a lack of change of original symptoms. If there is incontinence then no further treatment for BPE can occur and the only transitions possible are to death and from the 'remission, incontinence' state to the 'no remission, incontinence' state. If there is no incontinence and no remission and there are further treatments in the sequence then transition to the next treatment will occur. If the end of the treatment sequence is reached then the only transition that is possible is to the state of death. If there is no incontinence and remission then transition to 'no remission, no incontinence' can occur with the probability of relapse. This defines relapse as return to the original symptoms following an initially successful treatment.

All other complications are short term in that they are assumed to have resolved within the first 3 months post operation and are therefore included in the treatment state. The events considered are acute urinary retention (AUR), bladder neck contracture or urethral stricture (labelled BNC), blood transfusion, TUR syndrome and UTI.

All parameter values used to estimate the transition probabilities and probabilities of adverse short-term complications are given as expected values.

Separate tables are presented for cost and utility estimation in the relevant sections. Parameter distributions that are used in the Monte Carlo simulation can be seen in *Table 30*.

The epidemiology: parameterisation of the model

Effectiveness

Probability of failure (1)

In this subsection the method used to estimate the probability of failure (defined above as the transition from a treatment state to the 'no remission, no incontinence' or 'no remission, incontinence' states) of any treatment used on the first occasion is described. Its modification for repeating the same procedure in a strategy is described later in this chapter.

The challenge was to find a definition of failure that would be consistent for all treatments and a reliable method to estimate its probability. Therefore, given that the aim of treatment is to improve symptoms (LUTS), treatment failure was defined as 'insufficient improvement' in symptom score. 'Insufficiency' might be variably defined but, according to the clinical experts (R Pickard, University of Newcastle, J N'Dow, S McClinton, University of Aberdeen, 2006, personal communication), in clinical practice a percentage change of less than 10% in IPSS is most often used.

TABLE 30 *Parameter values (used to specify the Monte Carlo simulation in the DAM)*

Treatment	Event	Source	Expected value	SE	95% CI (except for uniform distributions)		Distribution type
					Low	High	
Baseline risk with TURP							
TURP	AUR	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.05	0.01	0.04	0.08	Beta
TURP	BNC	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.07	0.01	0.05	0.08	Beta
TURP	Incontinence	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.03	0.01	0.02	0.05	Beta
TURP	Transfusion	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.08	0.02	0.05	0.11	Beta
TURP	TUR syndrome	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.03	0.01	0.01	0.05	Beta
TURP	UTI	AUA meta-analysis (2003) (Francisca *et al*., 1999[86])	0.06	0.01	0.05	0.09	Beta
TURP	Failure at 12 months	Individual level data	0.06	0.02	0.03	0.09	Beta
Relative risks (TURP/treatment)							
HoLEP	AUR	Meta-analysis	0.71	NA	0.38	1.32	Lognormal
HoLEP	BNC	Meta-analysis	0.84	NA	0.43	1.65	Lognormal
HoLEP	Incontinence	Meta-analysis	0.82	NA	0.53	1.27	Lognormal
HoLEP	Transfusion	Meta-analysis	3.70	NA	1.05	14.29	Lognormal
HoLEP	TUR syndrome	Meta-analysis	3.24	NA	0.14	77.79	Lognormal
HoLEP	UTI	Meta-analysis	1.02	NA	0.32	3.23	Lognormal

Treatment	Event	Source	Expected value	SE	95% CI (except for uniform distributions)		Distribution type
					Low	High	
HoLEP	Failure at 12 months (model 2)	Meta-analysis	1.47	NA	0.69	3.13	Lognormal
KTP	AUR	Meta-analysis	2.89	NA	1.55	5.42	Lognormal
KTP	BNC	Meta-analysis	0.54	NA	0.32	0.90	Lognormal
KTP	Incontinence	Meta-analysis	1.17	NA	0.60	2.26	Lognormal
KTP	Transfusion	Meta-analysis	2.24	NA	1.03	4.88	Lognormal
KTP	TUR syndrome	Meta-analysis	0.14	NA	0.05	0.42	Lognormal
KTP	UTI	Meta-analysis	0.33	NA	0.01	7.93	Lognormal
KTP	Failure at 12 months (model 2)	Meta-analysis	1.68	NA	1.03	2.74	Lognormal
TUMT	AUR	Meta-analysis	1.64	NA	0.77	3.50	Lognormal
TUMT	BNC	Meta-analysis	0.20	NA	0.05	0.75	Lognormal
TUMT	Incontinence	Meta-analysis	1.64	NA	0.79	3.33	Lognormal
TUMT	Transfusion	Meta-analysis	9.09	NA	0.51	100.00	Lognormal
TUMT	TUR syndrome	Meta-analysis	5.83	NA	0.24	140.50	Lognormal
TUMT	UTI	Meta-analysis	0.95	NA	0.48	1.89	Lognormal
TUMT	Failure at 12 months (model 2)	Meta-analysis	0.50	NA	0.24	1.04	Lognormal
TUVP	AUR	Meta-analysis	2.12	NA	1.23	3.68	Lognormal
TUVP	BNC	Meta-analysis	0.91	NA	0.45	1.85	Lognormal
TUVP	Incontinence	Meta-analysis	0.92	NA	0.69	1.21	Lognormal
TUVP	Transfusion	Meta-analysis	0.19	NA	0.08	0.44	Lognormal
TUVP	TUR syndrome	Meta-analysis	0.59	NA	0.17	2.12	Lognormal
TUVP	UTI	Meta-analysis	0.65	NA	0.40	1.08	Lognormal

continued

TABLE 30 *Parameter values (used to specify the Monte Carlo simulation in the DAM) (continued)*

Treatment	Event	Source	Expected value	SE	95% CI (except for uniform distributions)		Distribution type
					Low	High	
TUVP	Failure at 12 months (model 2)	Meta-analysis	1.04	NA	0.53	2.07	Lognormal
Other risks							
TUMT	Failure of second treatment relative to first	Expert opinion	0.75	NA	0.50	1.00	Uniform
TURP	Failure of second treatment relative to first	Expert opinion	0.75	NA	0.50	1.00	Uniform
TURP	Pressure test positive	Expert opinion	0.75	NA	0.65	0.85	Uniform
Reoperation							
Any but TUMT and laser	Reoperation at 8 years	Madersbacher *et al.*, 2005[87]	0.08	0.00	0.07	0.08	Beta
TUMT	Reoperation at 5 years	Francisca *et al.*, 1999[86]	0.36	0.01	0.33	0.39	Beta
Baseline and relative mean IPSS scores							
Any	Pretreatment mean	Individual level data	22.08	0.47	21.16	23.01	Normal
Any	Successful treatment mean	Individual level data	6.61	0.38	5.86	7.35	Normal
HoLEP	WMD	Meta-analysis	0.42	0.05	0.32	0.52	Normal
KTP	WMD	Meta-analysis	–1.30	0.60	–0.12	–2.47	Normal
TUMT	WMD	Meta-analysis	–2.41	0.52	–3.42	–1.40	Normal
TUVP	WMD	Meta-analysis	–0.18	0.23	–0.63	0.26	Normal

Treatment	Event	Source	Expected value	SE	95% CI (except for uniform distributions)		Distribution type
					Low	High	
Utilities							
Any	AUR	Ackerman *et al.*, 2000[78]	0.88	0.00	0.22	0.23	Beta
Any	BNC	Ackerman *et al.*, 2000[78]	0.92	0.00	0.24	0.24	Beta
Any	Incontinence	Ackerman *et al.*, 2000[78]	0.88	0.00	0.22	0.23	Beta
Any	TUR syndrome	Ackerman *et al.*, 2000[78]	0.80	0.01	0.19	0.21	Beta
Any	UTI	Ackerman *et al.*, 2000[78]	0.92	0.00	0.23	0.23	Beta
Any	No remission	Kok *et al.*, 2002[273]	0.96	0.00	0.23	0.24	Beta
Any	Remission	Kok *et al.*, 2002[273]	1.00	0.00	NA	NA	Beta
Costing							
Any	Risk of TURP after AUR	Expert opinion	0.50	0.05	0.40	0.60	Beta
Any	Risk that incontinence is urge type	Expert opinion	0.95	0.02	0.91	0.99	Beta
Any	Baseline treatment (including mean LOS)	NHS reference costs, 2005[45]	1862.34	NA	1546.32	2195.54	Lognormal
Any	Urology ward bed day	NHS reference costs, 2005[45]	250.00	NA	141.00	443.26	Lognormal
Any	LOS of TUR syndrome	Expert opinion	2.00	0.51	1.00	3.00	Normal

continued

TABLE 30 *Parameter values (used to specify the Monte Carlo simulation in the DAM) (continued)*

Treatment	Event	Source	Expected value	SE	95% CI (except for uniform distributions)		Distribution type
					Low	High	
Any	LOS of UTI	Expert opinion	3.00	1.40	0.25	5.75	Normal
Any	Pressure test	NHS reference costs, 2005[45]	125.10	16.70	92.37	157.83	Normal
Any	Transfusion	Expert opinion	1270.00	323.98	635.00	1905.00	Normal
Any	Oxybutynin	Assumption	166	NA	65	267	Uniform
HoLEP	Life of machine	Expert opinion	10.00	NA	5.00	15.00	Uniform
HoLEP	Number of uses of HoLEP blade	Expert opinion	7.50	NA	5.00	10.00	Uniform
HoLEP	Number of uses of HoLEP fibre	Expert opinion	25.00	NA	20.00	30.00	Uniform
KTP	Life of machine	Expert opinion	10.00	NA	5.00	15.00	Uniform

AUA, American Urological Association; AUR, acute urinary retention; BNC, bladder neck contracture or urethral stricture; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; KTP, potassium-titanyl-phosphate; LOS, length of stay; NA, not available; TUMT, transurethral microwave thermotherapy; TUR, transurethral resection; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate; UTI, urinary tract infection; WMD, weighted mean difference.
The relative risks reported in this table are the reciprocals of those reported in the relevant systematic review chapters.

Formally:

Let $f(p)$ be the probability distribution of p in the population where p represents the relative change in symptom score pre and post surgery such that:

$$p = (I_{post} - I_{pre})/I_{pre} \quad (1)$$

where I_{post} is the IPSS score post surgery and I_{pre} is the IPSS score pre surgery.

Therefore, the probability of failure is given by:

$$P(\text{fail}) = P(p < x) \quad (2)$$

where x is the minimum percentage change in symptom score between pre and post surgery that would be considered sufficient (= 0.1).

Substituting (1) into (2) gives the probability of failure as:

$$P(\text{fail}) = P((I_{post} - I_{pre})/I_{pre}) < x) \quad (3)$$

where the probability of failure, P(fail), is equal to the probability that the percentage change in symptom score between pre and post surgery, $((I_{post} - I_{pre})/I_{pre})$, is less than x.

The main problem in estimating $P(p < x)$ from any effectiveness evidence is that these data are not reported and the IPSS scores are reported only as means of the whole sample at various points in time. Ideally, individual level data (ILD) for each treatment would be used but such data are unavailable. ILD were available, however, for two time points, pre treatment (baseline) and 4-month follow-up, for a sample of men from a study population (in particular, pretreatment IPSS > 7) who had received TURP (R Pickard, 2006, personal communication). Details of the characteristics of the patient population can be found in Appendix 11. The most reliable data comparing the effectiveness of TURP with other procedures should come from the estimates of the WMD derived from the meta-analysis (see Chapters 6–8). Therefore, the challenge was to estimate P(fail) for the other procedures using the ILD for TURP and the WMD for the comparison with TURP for each other procedure. This constituted 'model 1' for estimating the probability of failure. A second model was also developed. In model 2 the relative risks of retreatment obtained from the meta-analysis were used to estimate the relative risk of failure of each treatment compared with TURP. The results obtained from these two models were compared in a sensitivity analysis.

Model 1 (base case)

To estimate P_t(fail) for each treatment t, it is known that the mean IPSS score post treatment (as reported in a study) is equal to the average score of the mean of those who are successful and those who fail. This can be represented as:

$$\text{mean}_t(I_{post}) = P_t(\text{fail}) \cdot \text{mean}(I_{post})_{fail} + (1 - P_t(\text{fail})) \cdot \text{mean}(I_{post})_{success} \quad (4)$$

This formula can be rearranged to give the probability of failure for each treatment, P_t(fail):

$$P_t(\text{fail}) = (\text{mean}_t(I_{post}) - \text{mean}_t(I_{post})_{success})/(\text{mean}_t(I_{post})_{fail} - \text{mean}_t(I_{post})_{success}) \quad (5)$$

If it is assumed that the trial sample is similar to the ILD sample then the mean IPSS score post treatment for treatment t ($\text{mean}_t(I_{post})$) can be calculated as:

$$\text{mean}_t(I_{post}) = \text{mean}_{TURP}(I_{post}) - \text{WMD}_{tpost} \quad (6)$$

where $\text{mean}_{TURP}(I_{post})$ is the mean IPSS post treatment for TURP, and WMD_{tpost} is the weighted mean difference in IPSS post treatment for the comparison of treatment t with TURP.

Substituting equation (6) into equation (5) gives the following:

$$P_t(\text{fail}) = (\text{mean}_{TURP}(I_{post}) - \text{WMD}_{tpost} - \text{mean}_t(I_{post})_{success})/(\text{mean}_t(I_{post})_{fail} - \text{mean}_t(I_{post})_{success}) \quad (7)$$

In this equation $\text{mean}_{TURP}(I_{post})$ can be estimated from the ILD and WMD can be estimated from the meta-analysis. However, it is not known what the mean IPSS is for those who, by some definition, fail or have success. To solve this problem it was first assumed that a percentage change in IPSS of less than 10% ($x = 0.1$), given sample uncertainty, is equivalent to no change in symptoms, i.e. a proportion of individuals who are treated will be considered to have failed insofar as 'on average' they do not show any improvement in symptoms and this is independent of the initial IPSS.

The first assumption is, therefore, that the mean post-treatment IPSS of those who fail ($\text{mean}(I_{post})_{fail}$) is the same as the mean IPSS pre treatment ($\text{mean}(I_{pre})$) and is constant across all treatments, i.e.:

$$\text{mean}(I_{\text{post}})_{\text{fail}} = \text{mean}(I_{\text{pre}}) \quad (8)$$

Substituting equation (8) into equation (7) gives:

$$P_t(\text{fail}) = (\text{mean}_{\text{TURP}}(I_{\text{post}}) - \text{WMD}_{\text{tpost}} - \text{mean}_t(I_{\text{post}})_{\text{success}})/(\text{mean}(I_{\text{pre}}) - \text{mean}_t(I_{\text{post}})_{\text{success}}) \quad (9)$$

If it is further assumed that the mean IPSS post treatment for those for whom treatment was a success ($\text{mean}(I_{\text{post}})_{\text{success}}$) is constant across treatments then:

$$P_t(\text{fail}) = (\text{mean}_{\text{TURP}}(I_{\text{post}}) - \text{WMD}_{\text{tpost}} - \text{mean}(I_{\text{post}})_{\text{success}})/(\text{mean}(I_{\text{pre}}) - \text{mean}(I_{\text{post}})_{\text{success}}) \quad (10)$$

Both of these assumptions imply that the difference in mean IPSS between treatments (i.e. the WMD) is due only to a difference in the probability of failure and not to a difference in mean IPSS of those who are successful or mean IPSS of those who fail. This is convenient for the Markov model because it also means that the utility [which is a function of IPSS (see Utilities)] for the states of 'remission' and 'no remission' also does not vary between treatments.

When t is defined as TURP then the probability of TURP failing, $P_{\text{TURP}}(\text{fail})$, can be defined as:

$$P_{\text{TURP}}(\text{fail}) = (\text{mean}_{\text{TURP}}(I_{\text{post}}) - \text{mean}(I_{\text{post}})_{\text{success}})/(\text{mean}(I_{\text{pre}}) - \text{mean}(I_{\text{post}})_{\text{success}}) \quad (11)$$

Rearranging and substituting equation (11) into equation (10) leads to a definition of the probability of treatment t failing, $P_t(\text{fail})$, as:

$$P_t(\text{fail}) = P_{\text{TURP}}(\text{fail}) - (\text{WMD}_{\text{tpost}}/(\text{mean}(I_{\text{pre}}) - \text{mean}(I_{\text{post}})_{\text{success}})) \quad (12)$$

In the DAM, $P_{\text{TURP}}(\text{fail})$, $\text{mean}(I_{\text{pre}})$ and $\text{mean}(I_{\text{post}})_{\text{success}}$ were estimated from the ILD, and $\text{WMD}_{\text{tpost}}$ was estimated from the meta-analyses reported in Chapters 6–8. Because IPSS values in the meta-analysis continued to decline for up to 12 months post operation, it was assumed that this represented continued improvement. Therefore, the WMD at 12 months was used as the estimate of $\text{WMD}_{\text{tpost}}$.

Model 2

As for model 1 it was assumed that the treatments only differed by probability of failure and that those who failed had a mean IPSS post treatment that was the same as the pre treatment score and that those who were successful had identical post-treatment IPSS regardless of the treatment that they received. Probability of failure of TURP was also still estimated from the ILD. However, in model 2 the probability of failure of the other treatments was estimated from the retreatment relative risks estimate obtained as part of the review of effectiveness reported in Chapters 6–8. Of course, how the decisions to retreat were made in the trials is not known and they were perhaps not made according to the rule given above with regard to percentage change in IPSS.

Probability of failure (2): repeat and subsequent procedures

Given no other available evidence it was decided to estimate the probability of failure of subsequent, but different, procedures as if there was no previous history of treatment and subsequent repeat procedures according to a relative risk (RR):

$$P_{\text{tfail2}} = P_{\text{tfail}}/\text{RR}(P_{\text{tfail}}/P_{\text{tfail2}}) \quad (13)$$

where P_{tfail2} is the probability of failure of a second (repeat) procedure and the relative risk was estimated by clinical expert opinion (R Pickard, 2006, personal communication).

Probability of relapse

Relapse has already been defined in terms of the transition from the 'remission' state to the 'no remission' state. Again there is a lack of long-term data for all types of treatment and the data that are available are only in the form of the rate of retreatment. Also, because long-term retreatment is the sum of retreatment following relapse and retreatment following failure (as defined above), each relapse rate was calculated as the remainder from the total retreatment rate once the failure rate had been deducted, i.e.:

$$P_d(\text{relapse}) = P_{\text{td}}(\text{retreatment}) - P_t(\text{fail}) \quad (14)$$

where $P_d(\text{relapse})$ is the probability of relapse, $P_{\text{td}}(\text{retreatment})$ is the total probability of retreatment (including that following failure) over the time period d (obtained from the literature) and $P_t(\text{fail})$ is the probability of failure (estimated by either model 1 or 2).

All long-term probabilities were converted to transition probabilities by assuming a constant rate over the time period. Thus:

$$P_3(\text{relapse}) = 1 - (1 - P_d(\text{relapse})^{1/d})1 \quad (15)$$

Long-term data on retreatment were obtained for TURP for $d = 5$ years and for TUMT for $d = 8$ years. The other treatments were assumed to be

identical to TURP or TUMT depending on their short-term similarity as shown by the WMD in IPSS at 12 months. Thus, TUVP and HoLEP are the same as TURP and KTP the same as TUMT.

Complications (long and short term)

These are the probabilities for those complications occurring in the treatment state (AUR, BNC, transfusion, TUR syndrome and UTI) and incontinence. All non-TURP treatment complication probabilities were expressed in terms of a relative risk with respect to TURP and were based on data from the meta-analyses reported in Chapters 6–8. The baseline values for TURP were estimated by summing events across all TURP treatment arms of this meta-analysis. In the base case those from the UK were used and then compared with all studies.[85] Given the variability in reporting, the DAM has not attempted to differentiate between the different levels of severity of these events.

Utilities

The following equation expresses how the model calculates the discounted expected number of QALYs:

$$\text{Expected QALYs}_{\text{strategy}} = \Sigma\,(0.25 \cdot \text{EU}_{\text{cycle}} / (1+\text{discount rate})^{\text{cycle}}) \quad (16)$$

where EU_{cycle} is the expected utility of each cycle, i.e. the sum of the utilities of each state weighted by their probabilities, and '0.25' indicates that each cycle was a quarter of a year. Of course, the population total was estimated by multiplying the probability of each state counted post first treatment by the number of individuals from each cohort for each cycle and summing across all cohorts and all cycles. For example, during year 1 (1–2 years post technology introduction) there will be 25,000 new entrants, whose state transition probabilities are those of their first year post first treatment, plus 25,000 entrants who entered during year 0, whose transition probabilities will therefore be those of their second year post first treatment.

To estimate the utility of each health state it was necessary to express utility as a function of both LUTS and complications. As stated already, the states of 'no remission' and 'remission' are already defined in terms of IPSS, i.e. 'no remission' is the study population that have an IPSS greater than 7 and 'remission' is the mean IPSS of those who do not fail, as estimated from the ILD. Only one study[273] that maps IPSS to utility values could be found from the search for economic evaluations (which included studies reporting utility values).

However, although the clinical experts believed that by far the most important factor in making a treatment choice is LUTS, it was necessary to modify the utility values in the presence of any complications, for the incontinence states and for the within-treatment state complications (AUR, BNC, TUR syndrome and UTI). Therefore, what is first shown is how utility values are calculated for the states of 'no remission, no incontinence' and 'remission, no incontinence'.

Utility as a function of IPSS

Kok and colleagues[273] elicited preferences using an accepted method of time trade-off.[75] The sample was also fairly large ($n = 170$) and was composed of members of the general public (around Rotterdam in the Netherlands), which facilitates comparability with the use of utilities to calculate QALYs in other populations. In their analysis they mapped IPSS scores on to utility values such that $(L_o, L_i)_1$ is preferred to $(L_o, L_i)_2$ if and only if $U(L_o, L_i)_1 > U(L_o, L_i)_2$, where (L_o, L_i) is a set of levels, L_o referring to obstructive and L_i to irritative, each defined according to a range of the sum of the scores on either the obstructive or irritative domains of the IPSS measure. For example, $L_o = 1$ if $I_o <= 4$. The complete set of levels (derived in the Kok and colleagues study from factor analysis of the IPSS of 1414 patients over the age of 50 years newly referred in 13 hospitals in the Netherlands) is given in *Table 31*.

The resulting utility values are given in *Table 32*.

Therefore, each combination of obstructive and irritative scores can be mapped to a mean utility score.

Unfortunately, the IPSS values are only reported in the literature in the form of mean total scores, which are the sum of the irritative and obstructive domain scores. Therefore, an assumption is required as to the relative contributions of each of these domains to the total. In the absence of evidence it could be assumed that the observed proportion of the total IPSS of each of the domains is the same as the proportion of the maximum score, i.e. because $I_{\text{total}} = I_o + I_i$, where I_{total} is the total IPSS, I_o is the sum of the scores on the obstructive domains and I_i is the sum of the scores on the irritative domains, and because out of seven domains there are four obstructive to three irritative, each with the same maximum score, then $I_o = 4 \cdot I_{\text{total}}/7$ and $I_i = 3 \cdot I_{\text{total}}/7$.

TABLE 31 *Map of IPSS to levels on obstructive and irritative dimensions used to produce utility values (see* Table 32*)*

Domain	Summary score	Level
Obstructive		
Seldom/never	≤4	Obstructive 1
About half of the time/sometimes	≥5 and ≤16	Obstructive 2
Almost always	≥17	Obstructive 3
Irritative		
Seldom/never	≤3	Irritative 1
About half of the time/sometimes	≥4 and ≤9	Irritative 2
Almost always	≥10	Irritative 3

From this the utility of the state of 'no remission, no incontinence' can be estimated, as it is known that the mean IPSS estimated from the ILD is approximately 22. Therefore, if $I_{\text{total}} = 22$, $I_o = (4 \times 22)/7$ and $I_i = (3 \times 22)/7$, i.e. approximately $I_o = 13$ and $I_i = 9$, which, using the table of Kok and colleagues, maps to 2 on both the obstructive and the irritative domains. Using the algorithm provided by Kok and colleagues[273] these give a utility of 0.90, i.e. the utility of the preoperative state, which is also the state of 'no remission, no incontinence', is 'on average' 0.94. Similarly, for 'remission, no incontinence' the mean IPSS is estimated from the ILD to be about 6, which maps to a utility of 1, i.e. 'on average' successful treatment restores individuals to a state equivalent to full health. The ILD provided some support that I_o and I_i can be treated in the way described above in that they had a correlation coefficient of 0.4 and they occurred in approximately the same ratio preoperatively. Also, the mean utility estimated from the ILD both pre- and postoperatively was found to differ by less than 0.005 when estimated according to the assumption or when estimated using the actual data. Nevertheless, a sensitivity analysis tested the effect of using the minimum utility consistent with an IPSS of 7 for the state of remission. This corresponds to $I_o = 1$ and $I_i = 2$ (or vice versa) and, thus, using the data provided by Kok and colleagues a utility of 0.97 was estimated instead of 1.

Utility as a function of IPSS and non-LUTS factors

Only one study was found, by Ackerman and colleagues[78] (see Chapter 4), that estimated utility as a function of both LUTS and complications. The challenge was to 'map' these values to the Kok and colleagues utilities.[273] This was achieved by 'anchoring' to the state without complications by assuming that the state of 'moderate to severe' BPE described by Ackerman and colleagues was equivalent to the mean IPSS pre treatment (estimated from the ILD). This assumption can be justified because the definition of 'moderate to severe' is an IPSS > 7, which is also the IPSS in the study population. The Ackerman utilities for complications were then used in one of two forms, compared in a sensitivity analysis, either unadjusted or adjusted, by calculating them as:

$$U_{\text{Kok}}(\text{complication}) = U_{\text{Ackerman}}(\text{complication}) \cdot (U_{\text{Kok}}(\text{meanI}_{\text{pre}})/U(\text{moderate to severe})_{\text{Ackerman}}) \quad (17)$$

TABLE 32 *Utility values corresponding to obstructive and irritative levels (see* Table 31*)*

		Obstructive score		
		1	2	3
Irritative score	1	1.00	0.97 (0.11)	0.95 (0.09)
	2	0.97 (0.10)	0.94 (0.12)	0.92 (0.11)
	3	0.92 (0.15)	0.90 (0.14)	0.87 (0.14)

Data are expressed as mean (SD).

This, therefore, allows the estimation of the utility of a treatment state as the sum of the utility of the short-term complications (AUR, BNC, transfusion, TUR syndrome and UTI) that occur within this state weighted by their probabilities. Because incontinence can occur with or without remission from LUTS, there are two utilities: one for the state 'incontinence, no remission' and one for the state 'incontinence, remission'. It was assumed that the utility of 'incontinence, no remission' was equal to that for 'incontinence, remission' reduced by the 'disutility' (1−utility) of the 'no incontinence, no remission' health state. The effect of assuming that the utility of these states was the same was tested in a sensitivity analysis.

Costs

In keeping with the economic perspective, only costs applicable to the NHS in England and Wales have been included. The following formula expresses the discounted cost function estimated for each individual (thus excluding capital costs) for each treatment strategy:

$$\text{Expected cost}_{\text{strategy}} = \Sigma(\text{expected cost}_{\text{cycle}}/(1+\text{discount rate})_{\text{cycle}}) \quad (18)$$

As for QALYs, the total population costs were estimated by multiplying the probability of each state at each time post first treatment by the number of individuals from each cohort and summing across all cohorts and cycles. However, in addition, capital costs were included, which were the purchase of equipment that could be used by more than one individual and over several years. This category was assumed to apply only to HoLEP, TUMT and KTP. Also, as for utility, the cost of each state needs to be estimated. The states of 'no incontinence, remission' and 'no incontinence, no remission' incur no costs. The states including 'incontinence' ('incontinence, no remission' and 'incontinence, remission') incur the cost of treating incontinence. The treatment states incur the procedure cost and the cost of treating the short-term complications of AUR, BNC, transfusion, TUR syndrome and UTI. The cost of the procedures was also distinguished by:

- the length of stay of the procedure ($\text{LOS}_{\text{procedure}}$), which was taken to be separate from any extra LOS due to complications and which had a cost, $\text{cost}_{\text{LOSprocedure}}$
- the procedure cost (cost_{OP} excluding hospital stay but including perioperative ward time, investigations and theatre costs)
- complication costs ($\text{cost}_{\text{comp}}$)
- the cost of purchase of equipment for each individual ($\text{cost}_{\text{equipment}}$).

Therefore, the cost of the treatment state for treatment t is:

$$\text{Cost}_t = \text{cost}_{\text{tOP}} + \text{cost}_{\text{tLOSprocedure}} + \text{tcost}_{\text{equipment}} + \Sigma\text{cost}_{\text{comp}} \quad (19)$$

Procedure cost

Cost_{tOP} was assumed to be the same for all procedures. It was estimated by assuming that the 2005 NHS reference cost[45] [Health Care Resource Group (HRG) code L28 (without complications)] for the surgical treatment of BPE was the total treatment cost (including LOS due to initial procedure and complications). Cost_{tOP} was calculated by netting out the cost of LOS from NHS reference costs using the formula below:

$$\text{Cost}_{\text{OP}} = \text{cost}_{\text{reference}} - (\text{LOS}_{\text{reference}} \cdot \text{cost}_{\text{day}}) \quad (20)$$

where cost per bed day, cost_{day}, was estimated for a urological surgery ward from the NHS reference costs with HRG code L09 ('treatment of kidney or urinary tract infection') as this typically does not involve surgery. This cost was confirmed by estimating the difference in cost between HRG L27 (with complications) and L28 (without complications) and assuming that this difference was due mostly to the difference in LOS. $\text{LOS}_{\text{reference}}$ is the mean LOS given with the reference cost data for codes L27 and L28.

Although LOS estimates were retrieved from the meta-analysis it was the opinion of the experts that these largely reflected local practice and therefore the LOS of each procedure ($\text{LOS}_{\text{tprocedure}}$) was based on expert opinion of standard UK practice. Therefore, $\text{LOS}_{\text{tprocedure}}$ was assumed to be 3 days for TURP or TUVP, 2 days for holmium laser resection or laser vaporisation, and 0 days (day-case procedure) for TUMT. These values were varied in a sensitivity analysis.

In the absence of direct evidence the day unit cost of TUMT was estimated using expert opinion and evidence from several sources, including the lowest NHS reference costs for a day case and a local estimate (with cost elements removed to prevent the double counting of 'operation cost'). The cost was estimated to be between £200 and £400, with an expected value of £250 and most likely to be no more than £250 (the probability of being no more than £250 was 0.75).

TURP and TUVP were assumed to incur no additional equipment costs. For KTP, TUMT and HoLEP, additional costs of blades/fibres/probes were included. Costs of laser equipment were estimated from manufacturers (R Pickard, 2006, personal communication). The fibre/blade/probe costs per individual were calculated by assuming that for KTP and TUMT they are not reusable but for HoLEP they are. The number of reuses is expressed as a distribution based on expert opinion and manufacturers estimates (R Pickard, 2006, personal communication). All of the data used to calculate these costs are reported in *Table 30*.

Capital costs were those of the purchase of the machines and were estimated in the base-case model assuming efficient use at 250 uses per year with a lifetime consistent with that of the model of 10 years. Sensitivity analysis was conducted to reduce the number of uses per year. Travel costs were not included, as too few data were available on the siting of equipment.

Short-term complication costs

All costs of short-term complications were estimated based on expert opinion (R Pickard, personal communication 2006). More specifically, the cost of AUR was calculated as the cost of an additional day of LOS for 'trial without catheter' plus, for the proportion of patients who fail this trial (probability of TURP after AUR), the cost of TURP. The cost of BNC was assumed to be the cost of an additional TUIP. The cost of transfusion was calculated based on the cost of a unit of blood of £635 (R Pickard, 2006, personal communication) multiplied by the number of units (two on average). The cost of UTI was estimated as the cost of an additional LOS (3 days on average). The cost per bed day was $cost_{day}$ as estimated by the method described above.

Cost of incontinence

The cost of incontinence was calculated partly as a recurring cost of oxybutynin [from the British National Formulary (www.bnf.org/bnf/) on 3 November 2006; from 2.5 mg twice a day (£8.98 for 56-tablet pack) to 5 mg twice a day (£3.26 for 84-tablet pack)] multiplied by the proportion who would have urge incontinence, estimated as 0.95 by expert opinion. For the remaining 5%, incontinence was assumed to be cured by artificial sphincter, which incurred a one-off cost of £6000 (R Pickard, 2006, personal communication).

Accounting for uncertainty

Given that a systematic review and meta-analysis were included as part of this project, in estimating the parameter distributions for the Monte Carlo simulation, the starting point for all parameters was always an estimate of the expected value from the sample and a sampling distribution, which is equivalent to the likelihood. The clinical experts were asked to examine all of the estimates from the meta-analysis that informed the parameters in the DAM to see how credible the mean was as an estimate of population expected value and whether the size of the 95% confidence interval was a suitable estimate of the magnitude of uncertainty. When there was other sample evidence, such as from the ILD to estimate the probability of failure of treatment, the sampling distribution was also used. When no such data existed, the posterior used in the model was essentially a prior, estimated by expert opinion (R Pickard, 2006, personal communication) and checked by further expert opinion (J N'Dow, S McClinton, 2006, personal communication). The distribution was then estimated using an expected value and range, which implied an approximate 95% confidence interval, or, where there was greatest uncertainty, only a range, which implied a uniform distribution.

Table 30 contains a list of all parameters, their expected values, the standard errors and the confidence intervals along with a note of the distribution used and the source of data. All distribution shapes were chosen according to standard practice.[77] All relative risk estimates from the meta-analysis for complications and retreatment and for cost from the NHS reference cost data on procedure cost and LOS were log transformed to parameterise a symmetrical normal distribution. Beta distributions were parameterised from sample-based means and standard errors and used to estimate the uncertainty of parameters bounded by 0 and 1 (baseline probabilities and utilities). The normal distribution was parameterised from sample data using sample-based means and standard errors. This approach was used for IPSS estimation for the WMDs from the meta-analysis; the mean IPSS preoperatively ('no remission, no incontinence' state) and following successful treatment ('remission, no incontinence' state), both from the ILD; and the cost of the pressure test following the first TURP, from NHS reference costs.

When there were no sample data, the shape of the parameter distribution depended on some judgement as to the degree of uncertainty. Therefore, the normal distribution was parameterised by assuming that the expert opinion of upper and lower bounds corresponded to the 95% confidence interval. This approach was

used to estimate the uncertainty surrounding the LOS for TUR syndrome and UTI and the cost of transfusion. The beta distribution was similarly parameterised for estimating the uncertainty of the probability of requiring TURP because of AUR. A uniform distribution was used for the number of reuses of the HoLEP and laser fibres/blades and the lifetime of each of the machines as well as the probability of the pressure test showing obstruction.

The Monte Carlo simulation was run with 10,000 samples. The number of samples was chosen by trialling the Monte Carlo simulation with increasing numbers of samples to determine at which point the addition of further samples resulted in no changes in the strategies that were non-dominated and non-extendedly dominated as well as little effect on the incremental cost-effectiveness ratios (ICERs). Because the analysis was carried out at the 'population level', the expected value of perfect information (EVPI) was calculated immediately for an incidence of 25,000 per year over 10 years at a discount rate of 3.5%.

Results

The cost-effectiveness analysis

Table 33 shows the results of a Monte Carlo simulation with 10,000 samples.

TABLE 33 *Results of a Monte Carlo simulation with 10,000 samples*

Strategy	Cost (£)	Incremental cost (£)	Effectiveness (QALYS)	Incremental effectiveness (QALYS)	ICER
TUVP	£380,774,844		917,082		
TUMT	£387,042,593	£6,267,749	906,333	–10,749	(Dominated)
HoLEP	£400,549,783	£19,774,939	919,656	2574.1	£7682
TUVP/HoLEP	£413,712,972	£13,163,189	921,041	1384.8	£9505
TUVP/TURP	£416,466,605	£2,753,633	920,931	–109.3	(Dominated)
TUVP/TURP × 2	£418,264,231	£4,551,258	921,091	50.2	£90,576
TURP	£435,632,543	£17,368,313	918,222	–2868.7	(Dominated)
TURP × 2	£457,866,096	£39,601,866	920,340	–751.3	(Dominated)
TUMT/TUVP	£502,437,525	£84,173,294	919,219	–1871.9	(Dominated)
TUMT × 2	£504,459,471	£86,195,241	915,639	–5451.6	(Dominated)
TUMT/HoLEP	£509,607,654	£91,343,423	919,893	–1197.7	(Dominated)
TUMT/TUVP/HoLEP	£512,222,250	£93,958,020	920,231	–860.0	(Dominated)
TUMT/TUVP/TURP	£512,936,161	£94,671,930	920,203	–887.7	(Dominated)
TUMT/TUVP/TURP × 2	£513,448,707	£95,184,476	920,243	–848.0	(Dominated)
TUMT/TURP	£519,051,244	£100,787,013	919,281	–1810.1	(Dominated)
TUMT/TURP × 2	£525,599,769	£107,335,538	920,059	–1031.5	(Dominated)
TUMT × 2/TUVP	£543,805,485	£125,541,255	919,592	–1498.7	(Dominated)
TUMT × 2/HoLEP	£546,577,726	£128,313,496	919,798	–1292.5	(Dominated)
TUMT × 2/TUVP/HoLEP	£547,091,377	£128,827,147	919,896	–1195.2	(Dominated)
TUMT × 2/TUVP/ TURP × 2	£547,469,842	£129,205,611	919,899	–1191.8	(Dominated)
TUMT × 2/TUVP/TURP	£549,476,915	£131,212,685	918,172	–2919.0	(Dominated)
TUMT × 2/TURP × 2	£551,652,179	£133,387,949	919,846	–1244.7	(Dominated)
TUMT × 2/TURP	£556,354,850	£138,090,619	919,684	–1406.5	(Dominated)
KTP	£557,310,731	£139,046,500	907,708	–13,382.6	(Dominated)

HoLEP, holmium laser enucleation of the prostate; ICER, incremental cost-effectiveness ratio; KTP, potassium-titanyl-phosphate; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate

What is clear from the results presented in this table is that effectiveness increases (in terms of QALYs) when moving from performing only one treatment to repeating treatments or adding treatments on initial failure or later relapse in a strategy.

The strategy that would be considered cost-effective depends upon society's willingness to pay for a QALY. For example, if the threshold is £20,000 per QALY, then TUVP/TURP × 2 would not be cost-effective. However, if current practice is TURP × 2, i.e. TURP followed by another TURP as required, then TUVP/HoLEP and TUVP/TURP × 2 are both less costly and more effective. Therefore, a move from current practice to TUVP/HoLEP at such a threshold would follow from these results.

The cost-effectiveness acceptability curve (CEAC) (*Figure 30*) gives an indication of the amount of uncertainty surrounding point estimates of cost-effectiveness. Most of the strategies have a zero probability of being cost-effective. Assuming that society's willingness to pay for a QALY is £20,000, it is clear that not only is TUVP/HoLEP cost-effective 'on average' but also that it has a probability of about 0.8 of being cost-effective. If society's willingness to pay for a QALY is £80,000 then 'on average' TUVP/TURP × 2 would be most likely to be cost-effective. However the probability of being cost-effective is 0.5, similar to that of TUVP/HoLEP (*Figure 30*). Such uncertainty might affect the decision as to which strategy to implement. However, the CEAC should be interpreted with caution in that it does not reveal for each sample what the size of the differences in cost and effectiveness are.

Comparisons of all treatment strategies against a TURP alone as a common comparator

The data reported in *Table 33* were used to compare each individual treatment strategy with the strategy of TURP alone (i.e. patients all initially receive a TURP but should the procedure subsequently be deemed to have failed then the patient is managed non-surgically).

Table 34 shows the comparison of treatment strategies involving only a single surgery with TURP alone. For the comparison of TUMT or TUVP with TURP, TURP is more costly but more effective. The incremental costs per QALY for these two comparisons suggest that the savings obtained from a move from TURP to TUMT are probably not worth the loss of QALYs. Conversely, the savings that may be obtained from moving from TURP to TUVP may be worth the loss of benefits (the incremental cost per additional QALY provided by TURP compared with TUVP is greater than £30,000). HoLEP appears to be on average

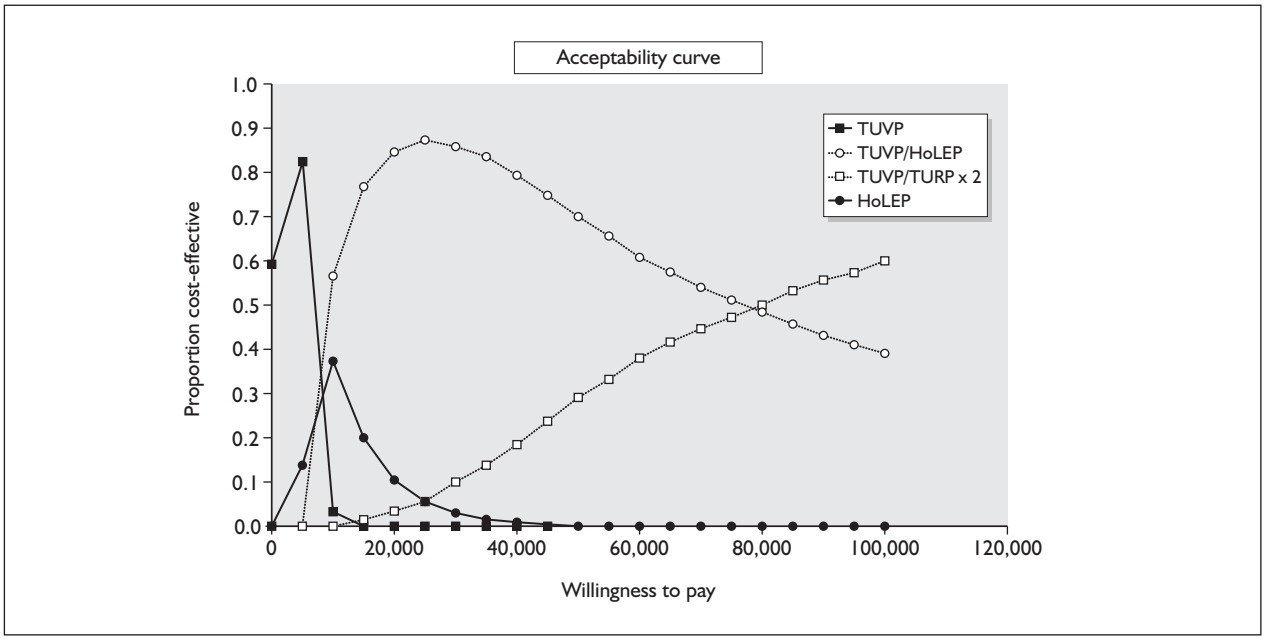


FIGURE 30 *Cost-effectiveness acceptability curve (Monte Carlo simulation with 10,000 samples).*

TABLE 34 *Comparison of single surgery strategies with the TURP strategy*

Comparison with TURP	Cost (£)		QALYs		Incremental cost (£)	Incremental QALYs	Incremental cost per QALY
	Alternative	TURP	Alternative	TURP			
TUMT	£387,042,593	£435,632,543	90,6333	91,8222	–£48,589,950	–11,890	£4087
HoLEP	£400,549,783	£435,632,543	91,9656	91,8222	–£35,082,760	1434	HoLEP dominant
KTP	£557,310,731	£435,632,543	90,7708	91,8222	£121,678,188	–10,514	TURP dominant
TUVP	£380,774,844	£435,632,543	91,7082	91,8222	–£54,857,699	–1141	£48,100

HoLEP, holmium laser enucleation of the prostate; KTP, potassium-titanyl-phosphate; QALY, quality-adjusted life-year; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

less costly and more effective than TURP alone (i.e. HoLEP is dominant) and KTP is less effective and more costly than TURP (TURP is dominant).

A similar comparison was made for those strategies involving a second surgery for those people for whom a first surgery was deemed to have failed (*Table 35*). TUMT × 2 is more costly and less effective than TURP (TURP is dominant). Other strategies involving TUMT as a first-line surgery are on average unlikely to be considered cost-effective.

Strategies involving TUVP as a first-line intervention were found to be less costly and more effective than TURP, continuing the trend started with the comparison of TUVP with TURP.

The final set of comparisons was for those strategies that allow more than one subsequent surgery if necessary (*Table 36*). The only strategies considered in this comparison were those in which the initial surgery was TUMT or TUVP. For all those strategies starting with TUMT, the incremental cost per QALY is at best on the borderline of what society might consider to be worthwhile, as would be expected given the analyses reported in *Tables 34* and *35*. The one strategy starting with TUVP is more effective and less costly than TURP alone.

Sensitivity analyses

Table 37 shows the results of one-way sensitivity analysis on a series of predetermined parameters. Varying the values for these parameters did not affect the set of non-dominated or non-extendedly dominated strategies. The exception to this was when the probability of treatment failure was based on the risks of reoperation and not changes in symptom scores. In this situation the use of HoLEP as a single treatment was excluded as it was extendedly dominated by the other treatment strategies considered. The reason for this is that the probabilities of failure all improved when the probability of treatment failure was based on the risks of reoperation and not changes in symptom scores. However, the probability of cost-effectiveness for HoLEP improved the least.

In all sensitivity analyses the ICERs are reported in *Table 37*. Any changes in ICERs are intuitively sensible. Whether these changes are sufficient to affect the choice of strategy depends again on society's willingness to pay for a QALY. However, in all cases but two a change from the status quo of TURP × 2 would be cost-effective. One case is if the LOS of TURP (exclusive of complications) were to be reduced from 3 to 2 days in line with that of TUVP. Here the decision would depend on the opportunity cost of moving to the more expensive but more effective TUVP/TURP × 2. In the other case, pressure testing is applied after TUVP as well as after TURP, which, although not standard practice, might be plausible and would thus makes TURP × 2 the most effective strategy. Although the ICER for TURP × 2 would be extremely high, given that it is already current practice it might be difficult to cancel the most effective although perhaps rather costly treatment.

Multiple cohort (population-based) versus single cohort (individual-based) model comparison

Table 38 shows the effect of estimating costs and QALYs for the entire population of men presenting for surgery at the rate of 25,000 per year for the next 10 years versus the effect of estimating costs and QALYs per individual from that population over 10 years, each starting now, discounted at

TABLE 35 *Comparison of strategies involving a second operation for patients for whom an initial operation fails with TURP*

Comparison with TURP	Cost (£)		QALYs		Incremental cost (£)	Incremental QALYs	Incremental cost per QALY
	Alternative	TURP	Alternative	TURP			
TURP × 2	£457,866,096	£435,632,543	920,340	918,222	£22,233,553	2117	£10,500
TUMT × 2	£504,459,471	£435,632,543	915,639	918,222	£68,826,928	–2583	TURP dominant
TUMT/HoLEP	£509,607,654	£435,632,543	919,893	918,222	£73,975,111	1671	£44,267
TUMT/TUVP	£502,437,525	£435,632,543	919,219	918,222	£66,804,982	997	£67,019
TUMT/TURP	£519,051,244	£435,632,543	919,281	918,222	£83,418,701	1059	£78,801
TUVP/HoLEP	£413,712,972	£435,632,543	921,041	918,222	–£21,919,571	2819	TUVP/HoLEP dominant
TUVP/TURP	£416,466,605	£435,632,543	920,931	918,222	–£19,165,938	2709	TUVP/TURP dominant

HoLEP, holmium laser enucleation of the prostate; QALY, quality-adjusted life-year; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

TABLE 36 *Comparison of strategies involving more than one repeat operation if required with TURP*

Comparison with TURP	Cost (£)		QALYs		Incremental cost (£)	Incremental QALYs	Incremental cost per QALY
	Alternative	TURP	Alternative	TURP			
TUMT/TUVP/HoLEP	£418,264,231	£435,632,543	921,091	918,222	–£17,368,312	2869	TUMT/TUVP/ HoLEP dominant
TUMT/TUVP/TURP	£512,222,250	£435,632,543	920,231	918,222	£76,589,707	2009	£38,129
TUMT/TUVP/ TURP × 2	£512,936,161	£435,632,543	920,203	918,222	£77,303,618	1981	£39,023
TUMT/TURP × 2	£513,448,707	£435,632,543	920,243	918,222	£77,816,164	2021	£38,510
TUMT × 2/TUVP	£525,599,769	£435,632,543	920,059	918,222	£89,967,226	1837	£48,970
TUMT × 2/HoLEP	£543,805,485	£435,632,543	919,592	918,222	£108,172,942	1370	£78,958
TUM × 2/TUVP/ HoLEP	£546,577,726	£435,632,543	919,798	918,222	£110,945,183	1576	£70,388
TUMT × 2/TUVP/ TURP	£547,091,377	£435,632,543	919,896	918,222	£111,458,834	1674	£66,602
TUMT × 2/TUVP/ TURP × 2	£549,476,915	£435,632,543	918,172	918,222	£113,844,372	–50	TURP dominant
TUMT × 2/TURP	£547,469,842	£435,632,543	919,899	918,222	£111,837,299	1677	£66,693
TUMT × 2/TURP × 2	£556,354,850	£435,632,543	919,684	918,222	£120,722,307	1462	£82,562
TUVP/TURP × 2	£551,652,179	£435,632,543	919,846	918,222	£116,019,636	1624	£71,441

HoLEP, holmium laser enucleation of the prostate; QALY, quality-adjusted life-year; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

TABLE 37 *Results of sensitivity analysis*[a]

Strategy	Cost (£)	Incremental cost (£)	Effectiveness (QALYs)	Incremental effectiveness (QALYs)	ICER
Base case[b]					
TUVP	£380,774,844		91,7082		
HoLEP	£400,549,783	£19,774,939	91,9656	2574	£7682
TUVP/HoLEP	£413,712,972	£13,163,189	92,1041	1385	£9505
TUVP/TURP × 2	£418,264,231	£4,551,258	92,1091	50	£90,576
Start age 90					
TUVP	£376,991,192		541,771		
HoLEP	£397,495,122	£20,503,931	543,268	1497	£13,695
TUVP/HoLEP	£405,702,102	£8,206,980	543,703	435	£18,872
TUVP/TURP × 2	£409,475,528	£3,773,426	543,715	12	£309,087
Start age 50					
TUVP	£381,248,895		1,002,040		
HoLEP	£400,940,948	£19,692,053	100,4857	2818	£6988
TUVP/HoLEP	£414,850,642	£13,909,693	100,6451	1594	£8727
TUVP/TURP × 2	£419,518,524	£4,667,882	100,6511	59	£78,771
Utility of 'incontinence, no remission' the same as utility of 'incontinence, remission'					
TUVP	£380,774,844		917,131		
HoLEP	£400,549,783	£19,774,939	919,679	2548	£7762
TUVP/HoLEP	£413,712,972	£13,163,189	921,092	1413	£9315
TUVP/TURP × 2	£418,264,231	£4,551,258	921,144	52	£88,045
Utility of IPSS < 8 is 0.97					
TUVP	£380,774,844		893,516		
HoLEP	£400,549,783	£19,774,939	894,844	1328	£14,889
TUVP/HoLEP	£413,712,972	£13,163,189	895,584	740	£17,791
TUVP/TURP × 2	£418,264,231	£4,551,258	895,611	28	£163,682
BPE risk data from all studies					
TUVP	£380,774,844		917,082		
HoLEP	£400,549,783	£19,774,939	919,656	2574	£7682
TUVP/HoLEP	£413,712,972	£13,163,189	921,041	1385	£9505
LOS TURP = LOS TUVP = 2 days					
TUVP	£376,715,152		917,082		
TURP	£380,679,392	£3,964,240	918,222	1140	£3476
TURP × 2	£400,362,758	£19,683,366	920,340	2117	£9296
TUVP/TURP × 2	£409,495,593	£9,132,834	921,091	751	£12,156
Probability of failure (model 2)					
TUVP	£380,793,296		918,558		
TUVP/HoLEP	£404,008,222	£23,214,926	921,217	2659	£8731
TUVP/TURP × 2	£406,972,673	£2,964,451	921,269	52	£56,845

continued

TABLE 37 *Results of sensitivity analysis[a] (continued)*

Strategy	Cost (£)	Incremental cost (£)	Effectiveness (QALYs)	Incremental effectiveness (QALYs)	ICER
Test for obstruction after TUVP[c]					
TUVP	£380,774,844		917,082		
HoLEP	£400,549,783	£19,774,939	919,656	2574	£7682
TUVP/HoLEP	£405,478,440	£4,928,657	920,051	395	£12,475
TUVP/TURP × 2	£409,175,523	£3,697,083	920,128	78	£47,659
TURP × 2	£457,866,096	£48,690,573	920,340	211	£230,608

HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; LOS, length of stay; QALY, quality-adjusted life-year; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.
a Based on 10,000 Monte Carlo simulation samples and showing non-dominated and non-extendedly dominated strategies only).
b Start age 70; utility of 'incontinence remission' = utility of 'incontinence, no remission' – disutility of 'no remission'; utility of IPSS < 8 is 1; BPE risk data from UK studies only; LOS TURP 3 days.
c The test is applied after TUVP only in strategies in which TUVP can be followed on failure by HoLEP or TURP. The test is also applied, as in the base case, before a second TURP *except* in the strategy TUVP/TURP × 2, in which it is has already been applied after TUVP.

3.5%. To make the comparison clearer, capital costs have been excluded. It has already been argued that the former (population-based) approach is the appropriate model for dealing with capital costs and therefore this sensitivity analysis is intended to show that there is also difference between the models excluding such costs because of the 'mixing' effect described above (see the beginning of Chapter 11).

It can be seen that the model does make a difference to the precise ICERs but that TUVP/HoLEP and TUVP/TURP × 2 are still more effective and less costly (not shown) than TURP × 2 (assumed to be current practice) and therefore the choice of strategy is between these strategies.

Expected value of perfect information (EVPI)

As described in Chapter 4 it is possible to use the DAM to estimate the value of reducing the uncertainty within the model and hence reduce the probability of making a wrong decision. Uncertainty can be reduced by obtaining further information and *Table 39* provides an indication of the value of reducing all uncertainty in the model

TABLE 38 *Comparison of multiple versus single cohort models*

	Cost (£)	Incremental cost (£)	Effectiveness (QALYs)	Incremental effectiveness (QALYs)	ICER
Individual based (single cohort model)					
TUVP	£1794		7.119357		
HoLEP	£1819	£25	7.139511	0.020154	£1242
TUVP/HoLEP	£1958	£139	7.152449	0.012938	£10,755
TUVP/TURP × 2	£1990	£31	7.152964	0.000515	£60,896
Population based (multiple cohort model)					
TUVP	£380,774,844		917,081.6		
HoLEP	£386,049,783	£5,274,939	919,655.7	2574.14	£2049
TUVP/HoLEP	£412,403,965	£26,354,182	921,040.6	1384.83	£19,031
TUVP/TURP × 2	£418,264,231	£5,860,266	921,090.8	50.24794	£116,627

HoLEP, holmium laser enucleation of the prostate; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

(i.e. our choice about which treatment or sequence of treatments is most cost-effective is based on perfect information). Also included in this table is the value of removing all uncertainty surrounding estimates of specific groups of parameters (the expected value of partial perfect information; EVPPI). The EVPI and the EVPPIs reported in *Table 39* are calculated at a threshold value for society's willingness to pay for a QALY of £20,000, given uncertainty as to its value.

What *Table 39* provides is an indication of the cost of the uncertainty, either overall (the EVPI) or in specific groups of parameters (EVPPI), and, therefore, the maximum value of future research that might be conducted to reduce this uncertainty. Parameter groupings such as utilities are not included because their EVPI was either extremely low or zero, i.e. their uncertainty had little or no effect on which strategy was cost-effective. It should be noted that this analysis does not reflect the value of improving model structure, for example the method of mapping IPSS on to utilities. It also assumes that the distributions around all of the parameters identified are accurate representations of the real uncertainty surrounding these parameter estimates.

Given an annual number of men undergoing TURP in the UK of 25,000, a discount rate of 3.5% and a £20,000 per QALY threshold, this places an upper limit on all future research investment of about £5.3 million over 10 years. If it is assumed that the sizes of the EVPPIs are directly proportional to the value of conducting further research then research focusing on improving the estimates of TUVP epidemiology (i.e. estimates of relative risks of complications and estimates of the WMD in IPSS relative to TURP) would have by far the highest priority. This could be achieved by undertaking more research comparing TUVP with TURP, perhaps within an RCT setting, with an upper limit on spending of about £4.1 million. The EVPI is highly sensitive to the willingness to pay for a QALY in that it almost doubles to £10.2 million on moving from £20,000 to £10,000 per QALY. This can be understood by observing that on the CEAC there is no clear 'front runner' at £10,000, which implies greatest uncertainty.

Consequences (disaggregated)

The cost-effectiveness analysis reported above aggregates the time spent in the various states of the model by the quality of life associated with these states. Although this has been carried out using the best evidence available and using explicit methods, further insight can be gained by considering the time spent in each of the states within the model for each treatment and treatment strategy considered (*Table 40*).

Table 40 shows that each strategy is associated with the same risk of death and hence the average time spent in that state is the same. The majority of time for each strategy is spent in the state of remission, although the average number of years spent in this state varies between 5.28 years for TUMT only and 7.92 years for TUVP/TURP × 2. Except for the strategy of KTP (0.21 years), the time spent in the state of incontinence is approximately a tenth of a year or less. Finally, the time spent in the state of no remission also varies considerably, with patients receiving TUVP/TURP × 2 and TUVP/HoLEP spending on average 0.05 of a year or less in this state and patients receiving a single TUMT spending on average over 2.74 years in this state.

In *Table 41* the different strategies are ranked in order of the time spent in two particular states: remission from LUTS and incontinence (the highest ranked strategy for remission is the strategy associated with the longest time spent in remission and the highest ranked strategy for incontinence is the one in which the least time is spent with incontinence). These two states are included as they are key determinants of the QALY estimates presented above. As this table illustrates there is no clear winning strategy. However, the CUA presented above suggests that the greater time

TABLE 39 *Expected value of perfect information (EVPI) at a threshold value for society's willingness to pay of £20,000*

Parameter group	EVPI (£)
All parameters (expected value of perfect information)	5,269,869
Expected value of partial perfect information (EVPPI)	
TUVP epidemiology	4,187,062
HoLEP epidemiology	1,652,886

HoLEP, holmium laser enucleation of the prostate; TUVP, transurethral vaporisation of the prostate.

TABLE 40 *Time in years spent in each state of the DAM for the base-case model ('incontinence' includes 'incontinence, no remission' and 'incontinence, remission')*

	Operation	Remission	No remission	Incontinence	Death	Total
TUMT	0.25	5.28	2.74	0.06	1.67	10
TUVP	0.25	7.27	0.72	0.09	1.67	10
KTP	0.25	5.65	2.21	0.21	1.67	10
TURP	0.25	7.44	0.55	0.09	1.67	10
HoLEP	0.25	7.65	0.33	0.09	1.67	10
TUMT × 2	0.35	6.82	1.08	0.08	1.67	10
TUMT/TUVP	0.35	7.56	0.33	0.08	1.67	10
TUMT/TURP	0.35	7.61	0.27	0.09	1.67	10
TUVP/TURP	0.27	7.89	0.07	0.09	1.67	10
TURP × 2	0.26	7.78	0.18	0.10	1.67	10
TUMT × 2/TUVP	0.40	7.62	0.23	0.08	1.67	10
TUMT × 2/TURP	0.40	7.63	0.21	0.09	1.67	10
TUMT/TUVP/TURP	0.36	7.75	0.13	0.09	1.67	10
TUMT/TURP × 2	0.36	7.71	0.16	0.09	1.67	10
TUVP/TURP × 2	0.27	7.92	0.04	0.09	1.67	10
TUMT × 2/TUVP/TURP	0.40	7.68	0.16	0.09	1.67	10
TUMT × 2/TURP × 2	0.40	7.67	0.17	0.09	1.67	10
TUMT/TUVP/TURP × 2	0.36	7.75	0.12	0.09	1.67	10
TUMT × 2/TUVP/TURP × 2	0.40	7.68	0.16	0.09	1.67	10
TUMT/HoLEP	0.35	7.68	0.21	0.09	1.67	10
TUMT × 2/HoLEP	0.40	7.66	0.19	0.09	1.67	10
TUVP/HoLEP	0.27	7.91	0.05	0.09	1.67	10
TUMT/TUVP/HoLEP	0.36	7.75	0.12	0.09	1.67	10
TUMT × 2/TUVP/HoLEP	0.40	7.68	0.16	0.09	1.67	10

HoLEP, holmium laser enucleation of the prostate; KTP, potassium-titanyl-phosphate; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

spent in remission tends to be more important than the shorter time spent in the state of incontinence. Therefore, the findings of the CUA that TUVP/TURP × 2 is the most effective in terms of QALYs are perhaps to some extent validated by this analysis.

Summary

In this chapter our DAM has been presented, which responded to the issues raised by the critique of previous DAMs reported in Chapter 4. The results show that the least costly treatment is TUVP followed by TUMT and then HoLEP but that TUMT is less effective than TUVP and HoLEP is more effective than TUVP. However, HoLEP might not be considered to be the most cost-effective when balancing all relevant complications with LUTS improvement as shown by the use of QALYs. This is because no treatment is 100% effective and the use of the most effective single treatment of HoLEP is believed to preclude any further treatment that might otherwise 'mop up' those who fail. Therefore, treating with a less effective, but nonetheless still very effective, treatment that allows further treatment should there be failure might be the best option. This approach has the advantage of most men achieving effective symptom relief with reduced complications and lower cost, although a few men would be disadvantaged by needing a further, more invasive treatment.

Whether this is indeed the case and what sequence of treatments is optimal depends on two major factors, the 'true' outcomes of the procedures and society's willingness to pay for a QALY. What is

TABLE 41 *Ranking of strategies by time spent in state (best first)*

Rank	Remission	Incontinence
1	TUVP/TURP × 2	TUMT
2	TUVP/HoLEP	TUMT × 2
3	TUVP/TURP	TUMT/TUVP
4	TURP×2	TUMT × 2/TUVP
5	TUMT/TUVP/TURP × 2	TUMT × 2/HoLEP
6	TUMT/TUVP/HoLEP	TUMT × 2/TUVP/HoLEP
7	TUMT/TUVP/TURP	TUMT × 2/TUVP/TURP
8	TUMT/TURP × 2	TUMT × 2/TURP
9	TUMT × 2/TUVP/TURP × 2	TUMT × 2/TUVP/TURP × 2
10	TUMT × 2/TUVP/HoLEP	TUMT/HoLEP
11	TUMT × 2/TUVP/TURP	TUMT × 2/TURP × 2
12	TUMT/HoLEP	TUVP
13	TUMT × 2/TURP × 2	TUMT/TUVP/HoLEP
14	TUMT × 2/HoLEP	TUMT/TURP
15	HoLEP	TUMT/TUVP/TURP
16	TUMT × 2/TURP	TUMT/TUVP/TURP × 2
17	TUMT × 2/TUVP	TUMT/TURP × 2
18	TUMT/TURP	HoLEP
19	TUMT/TUVP	TURP
20	TURP	TUVP/HoLEP
21	TUVP	TUVP/TURP
22	TUMT × 2	TUVP/TURP × 2
23	KTP	TURP × 2
24	TUMT	KTP

HoLEP, holmium laser enucleation of the prostate; KTP, potassium-titanyl-phosphate; TUMT, transurethral microwave thermotherapy; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporisation of the prostate.

the appropriate level of society's willingness to pay for a QALY is unclear as it depends upon the opportunity cost of the resources required to obtain an additional QALY, which is unknown. As for the first factor, this study has attempted, through economic and statistical methods, to represent the beliefs of decision-makers, informed by the best evidence, regarding the relationship between the outcomes and each strategy. As stressed earlier in this report, there are considerable limitations in the current evidence base for estimating effects and so the values used in the DAM may be subject to considerable uncertainty. Nevertheless, the base-case results should provide a basis to inform the current decision as to which technology should be implemented. Should it be shown that it is affordable then the model suggests that the best strategy would be TUVP followed, if necessary, by up to two TURPs. In practice, however, these results should be interpreted with caution and the data on which they are based are probably not strong enough to warrant a change in NHS practice from the TURP × 2 strategy. However they do indicate that strategies of HoLEP alone and TUVP followed by HoLEP (TUVP/HoLEP) might be worthy of further consideration.

The value of perfect information results indicate that it might be worth considering further research to better inform a decision in the future and also to determine the relative priorities of the types of evidence that need to be gathered. It should be noted that the results presented depend upon the imprecision around estimates being fully incorporated into the model. Nevertheless, the results indicate that it may be worthwhile gathering further evidence to compare TUVP and TURP.

Chapter 11
Discussion

In common with other areas of medicine the surgical treatment of BPE has undergone rapid technological change in recent years. Routine application of such new technology is dependent on many factors but is ideally governed by demonstration of benefit over existing standard treatment, in this case TURP. A systematic review of interventions with meta-analysis of available data and an economic evaluation was undertaken to determine whether any of the currently available newer technologies provide greater effectiveness, fewer complications and greater cost-effectiveness than TURP.

Summary of results

In respect of symptoms associated with BPE we found that TURP provides a consistently high level of improvement, which persists in the long term. This is associated with significant improvement in quality of life and peak urine flow rate. Of the newer technologies, minimally invasive options such as TUMT and TUNA result in less symptom improvement and a smaller increase in peak urine flow rate. Ablative procedures such as TUVP and laser resection (HoLEP) give similar symptom and quality of life improvements to TURP, and HoLEP additionally results in a greater improvement in flow rate (WMD + 1.43 ml/s at the 12-month follow-up). Purely in terms of effectiveness, HoLEP would appear to be unique amongst the newer technologies in offering an advantage over TURP, although, based on the current short-term outcome data available, this is confined to the urodynamic outcome, which may not be of importance to patients. Longer-term outcome data are keenly awaited. Reduction in hospital stay for elective surgery is currently considered to provide benefit to the patient in terms of avoiding complications and to the care provider in terms of reducing costs. Some of the newer technologies take longer to carry out but in the UK and the US context may result in a reduction in stay of up to 1 day, although this may be associated with a more prolonged period of catheterisation at home. It should also be noted that hospital stay for TURP is also shortening, from 5–6 days in the older trials to 3 days in the more contemporary ones. The impact of increased operating time and reduced hospital stay will vary between care providers and different health-care systems.

The search for alternative methods of prostate ablation has been fuelled largely by the risk of adverse consequences of bleeding during and after conventional TURP. This is a particular issue because excessive blood loss and the requirement for irrigation during the procedure may contribute to perioperative risk, particularly for elderly men who often have pre-existing cardiovascular disease. Our review confirmed that severe blood loss, as indicated by the need for blood transfusion, was more common amongst men randomised to TURP than amongst those undergoing most, if not all, other interventions. It should be noted, however, that contemporary studies such as those involving HoLEP show much lower rates of transfusion after TURP than older studies, suggesting beneficial changes to the performance of standard surgery over time.

The situation regarding complications that cause continued disability and hence that can be assumed to have an adverse effect on quality of life with associated ongoing health-care costs is much less clear. Sexual side effects of surgery, particularly loss of ejaculation and erectile dysfunction, are also of concern to men undergoing prostate surgery. The risk of retrograde ejaculation is significantly lower for minimally invasive procedures and TUIP, presumably indicating relative preservation of the preprostatic sphincter. For ablative procedures, perhaps not surprisingly, the risk is similar to that of TURP. Reassuringly, the occurrence of ejaculatory dysfunction does not seem to cause much in the way of quality of life impairment following prostate surgery. Rates of erectile dysfunction were similar across all procedures although lack of baseline data is a likely source of bias. The lack of effect of prostate surgery on this aspect of sexual function is supported by data from trials including a no intervention arm.[6] The rate of incontinence, the adverse effect most feared by men undergoing surgery for BPE, was similar across all interventions with the exception of TUNA and laser coagulation (for which reported rates were lower), although comparative analysis

was hampered by variability in definition. This finding is perhaps expected because all of the tissue ablative procedures follow the concept of removing prostate tissue to achieve benefit and therefore have the same risk of sphincter damage or pre-existing bladder dysfunction. The other most pertinent long-term adverse effect is the need for further treatment as a result of stricture formation, urinary retention or disease relapse. Unfortunately, as is frequently the case, these were not primary outcome measures in any of the RCTs and the necessary long-term follow-up data were either missing or incomplete. Difficulty passing urine after surgery reflected by the complication of acute retention together with the later need for reoperation was, however, more frequently seen with newer technologies, especially the minimally invasive interventions, which probably reflects the generally smaller amount of tissue removed or ablated by these procedures. This contention is supported by results from trials using HoLEP, in which the extent of prostate removal is similar to that of TURP, which is reflected in equivalent rates of retention and reoperation.

The results of the review of effectiveness were, along with other relevant data (e.g. on costs and utilities), combined in an economic model (the DAM). The purpose of the DAM was to determine which single surgical treatment or sequence of surgical treatments for BPE would be considered most likely to be cost-effective. The DAM can be thought of as a further level of evidence synthesis as it sought to combine the best available evidence to provide estimates of costs, effectiveness (measured in terms of QALYs) and cost-effectiveness. The results of the DAM suggest that the treatment or sequence of treatments that would be considered cost-effective is dependent upon what value we think society would be willing to pay to obtain an additional QALY. The most effective single treatment was HoLEP. However, the most effective strategy was TUVP/TURP × 2. The difference between these appears to be small on average, but the crucial issue is whether society is willing to pay for this gain in effectiveness.

HoLEP as a single treatment was found to be cost-effective for a willingness to pay of up to about £4556 per QALY. Up to £47,221 per QALY, TUVP followed by HoLEP would be considered cost-effective. Only at higher values for society's willingness to pay would one choose the most effective strategy, i.e. TUVP/TURP × 2. However, the story does not end there because, even if we believe that these results reflect our beliefs as informed by the best available evidence, there remains uncertainty. This was represented in a probabilistic way and can be observed partly in the CEAC and also in the EVPI and EVPPI. The CEAC shows that, at a willingness to pay of about £20,000, there is little doubt that TUVP/HoLEP is cost-effective. However, there are peaks of uncertainty at about £5000 and £50,000 and at these values for society's willingness to pay for a QALY, EVPI and EVPPI are highest, particularly at a threshold of £5000 per QALY. If one believes that the current threshold for the NHS is about £20,000, which is probably conservative, then it would seem reasonable to recommend changing from the current practice of a single TURP to TUVP/HoLEP. However, the economic model should be interpreted cautiously because of the assumptions and uncertainties that underpin it as well as the threshold value for society's willingness to pay for a QALY.

These results are consistent with the finding of the systematic review of effectiveness. It is important to note that even relatively modest changes in the parameter estimates used in the DAM might change these results because there are few data available for many of the comparisons and, as a result, estimates of effectiveness (and hence cost-effectiveness) will change as new data become available.

Strengths and weaknesses of the review of clinical effectiveness

The strength of the study is the systematic approach taken to review the evidence (published and unpublished data without language restrictions). Exhaustive systematic searches were made of the major electronic databases. All potentially eligible studies were reviewed for eligibility and the study quality assessed. Outcome parameters were predetermined and data were extracted using standard forms. Despite these efforts it is possible that some relevant and usable data remained hidden as a result of non-publication.

Moreover, more than half of the available evidence was reported in abstract form rather than in full-text published studies. The difficulties in accessing raw or summarised data from studies reported only in abstract form are well recognised and the process was beyond the funding limits of our review. The exclusion of these studies prevents

us from estimating the impact of this form of publication bias on the results. The reasons why so many trials were only reported as abstracts were unclear and ideally should be investigated because publication bias has been shown to account for up to 45% of an observed association, which may change the direction of effect.[274]

Empirical research in other fields has shown that unpublished reports tend to show less positive results than published reports, and so exclusion of these could introduce publication bias. In total, 88 full-text primary RCTs were identified. Although this haul of relevant trials is impressive, the majority of studies recruited small numbers of patients and covered many different comparisons, diluting the opportunities for meta-analysis. The confidence intervals around estimates of differences were often wide and this problem may result in a failure to demonstrate statistical significance for a clinically important effect or a failure to rule out an effect when it does not exist.[275,276]

Another major limitation resulted from the fact that the majority of comparisons were made against TURP, with few head-to-head comparisons of the newer technologies. Study inclusion criteria also varied considerably between the trials, which calls into question the generalisability of the findings on meta-analysis to 'everyday practice'. This was exacerbated by variation in operative technique and treatment protocols between studies investigating the same technology. These variations were of particular concern in studies involving laser technology, in which there was variation in power settings and temperature, together with site and duration of laser application. The limited descriptions of technologies in some study reports made it hard to determine whether they were minimally invasive or tissue ablative. This is an important possible explanation for the statistical heterogeneity that was common in the analysis. The long time base of the studies reviewed (20 years) in the context of rapidly changing and evolving technology also presents difficulties in interpretation of the findings. To overcome this we categorised interventions conceptually according to the mechanism of treatment of BPE between standard, minimally invasive and tissue ablative. Despite this the ablative group does have a range of tissue effects from partial vaporisation to complete resection. In addition, the standard of conventional TURP has not been static over this time frame. Developments in camera and televisual display and diathermy generators, improvements in perioperative care and concentration of the procedure in the hands of specialist urologists have all served to make the operation more uniform in outcome and less morbid in terms of adverse effects. All of these factors are likely to influence the findings. Although the review attempted to identify and explore sources of variability, for many outcomes it remained unclear as to whether any conclusions should be drawn from the results given the high statistical heterogeneity that was present.

The role of quality assessment in the conduct of a systematic review is important. For this review a robust combined checklist assessing different sources of bias was produced. We avoided using a scoring scale approach as this has been reported to be inaccurate concerning the direction of bias[277,278] and can include items that are unrelated to the internal validity of a study.[279] In this review we found that the majority of included RCTs were poorly reported, which may be associated with low levels of methodological quality.[279] There are a number of mitigating factors such as space limitations in the publishing journals but it is a generally held view that if necessary information is not provided then the quality will always be inadequate.[280] Without adequate reporting, assessing quality becomes impossible,[281] and the drive to ensure adherence to standardised conduct and reporting guidelines for RCTs has much to commend it from the point of view of the systematic reviewer.[88] It is also of concern that reporting of allocation concealment was unclear in 74% of the included studies and 14% used an inadequate approach to concealment of randomisation. This increases the risk of selection bias by disrupting the assignment sequence and may result in loss of the advantages of randomisation.[282] The main consequence of this is thought to be the generation of larger estimates of treatment effects.[281] An observational study that assessed methodological quality of 250 RCTs from 33 meta-analyses found that odds ratios were exaggerated by 30% for trials with unclear concealment protocols.[281] There were also differences between trials with regard to baseline characteristics. For example, studies comparing the efficacy and safety of laser resection with the efficacy and safety of TURP included patients with large prostate glands, whereas those assessing laser vaporisation included patients with a wide variation in prostate size. Variations such as these make the results difficult to interpret.

Blinding of patients, outcome assessors and care providers is another important methodological issue and reporting of this was unclear in more

than 70% of the studies. For the present review, obvious differences in the technologies make blinding of the patient and operator difficult, but the outcome assessor could be blind to the allocated treatment and trial reports should include a description of the attempts made to prevent ascertainment bias.

Many studies failed to report point estimates and measures of variability, which hinders calculation of the precision of the overall pooled estimate and calculation of weighted mean differences when standard deviations are required.[283] In this review of effectiveness, when an appropriate measure of variability was not reported for continuous outcomes, consistency across studies reporting the outcome was investigated. Methods to derive an estimate of standard deviation have been described, based on the imputation of plausible values, but doubts as to their validity exist as many have not been theoretically derived or empirically tested.[283] It is possible that if means and standard deviations were reported more consistently, effect sizes would be different. This is another reason why adherence to CONSORT guidelines for reporting of clinical trials greatly aids the conduct of robust meta-analyses.

A more specific methodological limitation that frustrated pooled analysis was the use of differing measures of symptomatic outcome in the older studies. We did attempt to convert the older and now little-used Madsen–Iversen symptom score to the present standard of AUA/IPSS using a method suggested by Barry and colleagues[284] but found that the results lacked reliability. This problem forced us to analyse studies using the Madsen–Iversen index separately, so reducing the power of the meta-analyses.

In summary, we believe that we have used the best available techniques to identify, review and meta-analyse the data that were available to us. This approach has enabled us to make robust broad conclusions concerning the relative beneficial and adverse effects of new technologies for the invasive treatment of symptomatic BPE compared with the standard of TURP. Our ability to consider infrequent complications and achieve precise separation of the different procedures according to relative effectiveness was limited by the small numbers of patients studied, inadequate reporting of trials, the use of differing outcome measures and the pace of technological development.

Strengths and limitations of the DAM

The DAM chapter provides an explicit and detailed description of the method used. It sought to use a set of criteria to identify which treatments and strategies were clinically plausible for the UK and these were then compared in terms of their costs and consequences. The pathways, developed following detailed discussions with the clinical experts involved in the study, were used to structure the economic model and identify which data would be required to parameterise the model. The methods used to obtain the parameter estimates were explicit and systematic and sought to identify the best data available. When assumptions were made about which data to use or how they would be used in the model, these have been described and justified, and, when necessary, they were tested in sensitivity analyses. This sensitivity analysis was conducted deterministically when appropriate, along with probabilistic sensitivity analysis. The probabilistic sensitivity analysis and probability distributions for all relevant parameters were obtained using explicit methods that met current guidelines for best practice in economic modelling.[285]

Despite our best efforts to conduct a rigorous economic evaluation using the best methods and data available, the results of the economic model should be interpreted cautiously because of the uncertainties and assumptions that underpin it. In particular, as described in the previous subsection, the evidence on effectiveness is limited because of the paucity of the available evidence base. As these data formed many of the input parameters of the DAM, this leads to uncertainties in the results obtained from the DAM. As indicated above, when possible, data inputs to the DAM and assumptions were tested in sensitivity analyses. In addition, when appropriate, parameters were estimated as distributions. These distributions were based on the available data and on guidelines for best practice and attempted to account for the imprecision surrounding the point estimates used within the DAM. It is still, however, contestable whether the parameter estimates and their associated distributions are an accurate measure of the true values of the parameters. However, although the data used were the best available and all distributions were examined in terms of summary statistics (expected value and confidence intervals) by the clinical experts to test their face validity, it is

possible that the available data are biased. This is because, as described earlier, the data contributing to the pooled estimates of effectiveness were incomplete and heterogeneous. When sampling data were not available, distributions were constructed in a pragmatic way; however, expert opinion was always sought. Extensive one-way sensitivity analysis was also used to reveal parameters when the decision was sensitive to variability within the range of a distribution.

In addition to the limitations caused by the evidence base, the economic evaluation suffers from a number of other limitations. First, conclusions about cost-effectiveness are sensitive to the value that we think society might be willing to pay for an additional QALY. Although there have been some attempts to define what this value might be,[286] in this report we do not explicitly identify the opportunity cost (i.e. the benefits forgone) of redeploying resources to provide a more costly but more beneficial procedure.

The model attempted to compare many different strategies, indeed many more than any previous evaluation in this area. Nevertheless, it was not possible to include every permutation of treatments. Therefore, a series of judgements had to be made about which strategies to present. This judgement was informed by discussions with the surgeons involved in the project team. Thus, twenty strategies were compared within the model and the reasoning behind including these strategies was explicit, with justification based on expert opinion and logic.

One of the determinants of cost-effectiveness was the probability of treatment failure. Within the model, assumptions had to be made as to how best to define treatment failure. For the base-case analysis, the definition used for treatment failure was based on clinical criteria relevant to the UK (the percentage change in IPSS). However, this created problems in terms of estimating probabilities of failure from the literature in cases in which only reoperation rates were available and the criteria for reoperation used in the different studies were either unknown or variable. A method was found to solve this problem whereby the best available evidence, i.e. weighted mean differences from the meta-analysis, was used, but it necessitated the use of observational individual-level data and the use of certain contestable assumptions. Therefore, the results of this analysis were compared with the results obtained when the failure was defined using reoperation rates. The results using these two different approaches were reassuringly consistent.

IPSS scores were also central to the estimation of QALYs. More specifically it was believed that utility scores that underpin the QALY estimates should be related to IPSS as well as to the presence or absence of complications. However, no single reliable source could be found that would allow us to do this. Thus, a set of assumptions to synthesise data from various sources were made. Some of these assumptions are contestable but they were tested in the sensitivity analysis and were found, on the whole, not to affect outcome. Perhaps more importantly, the estimation of QALYs relied on a mapping exercise from IPSS on to utility scores. There was no alternative source of such data and there may be concerns over the validity and usefulness of the estimates it produced. The estimates of EVPI did not capture the effect of removing this uncertainty as no probability distribution was specified. However, it is likely that further research into the mapping of IPSS on to health state utilities would be warranted.

Estimates of cost were not always easy to obtain; however, this study provided a breakdown of costs that was sufficient to estimate the independent effects of procedure cost, hospital inpatient stay and purchase of any new equipment. Nevertheless, costing by all resource categories was not possible. Therefore, a judgement was made as to those resource categories that were most likely to produce a difference in the decision. These judgements were informed by data that were relevant to the UK including the NHS reference costs. However, the NHS reference costs are not provided for all relevant treatments and, indeed, largely refer to TURP only. They also include a length of stay component that not only is a function of the complications of treatment but also reflects variations in practice. Therefore, methods were used to replace the length of stay component of these costs with length of stay costs based on typical length of stay (based on clinical opinion) and the cost of a day in hospital on a urology ward. It was also assumed, on the basis of availability in a typical institution, that TURP and TUVP would incur no additional equipment costs but that TUMT, HoLEP and KTP would. All of these assumptions were tested in sensitivity analyses.

The incorporation of complications into the model was also problematic. For example, there were no standard reference costs available for the management of complications and, therefore, expert opinion was used to inform the cost of these

events. The likelihood of complications occurring (i.e. the event probabilities) was also important for the model. These probabilities were estimated using the best available source, i.e. relative risks and pooled baseline TURP probabilities from the meta-analysis. They are limited, nevertheless, by the imprecision of the estimates, the possibility of population heterogeneity, variability in reporting and uncertainty in the time frame over which these events might occur. Thus, it was assumed that all complications except incontinence were short term and that all cases of incontinence were of urge incontinence (although it is possible that some cases may in fact be stress urinary incontinence), which was assumed to be permanent. Again, these assumptions were explicit and justification was provided.

In summary, the DAM has sought to use the best available data relevant to the UK and combined it within an explicit model that was again structured to reflect the costs and consequences of treatments and treatment strategies potentially relevant to the UK. Although the results of the DAM should be treated cautiously, we believe that the results provide the best evidence on cost-effectiveness of surgical treatments for BPE available to the UK.

Chapter 12
Conclusions

Implications for practice

Based on current evidence it is not possible to reliably identify the most promising minimally invasive intervention, although, as a group, these interventions are less effective than TURP but are associated with fewer adverse effects. It is similarly not possible to reliably identify the most promising tissue ablative intervention for the reasons described above. TURP continues to be effective although is associated with potentially significant morbidity. Each of the surgical interventions for BPE has advantages and disadvantages. Irrespective of the choice of intervention, the true cost to patients and society in terms of quality of life has not been quantified to date. Given that there are broad similarities in clinical effectiveness of the minimally invasive and tissue ablative interventions, perhaps the most important issue is whether patients would prefer to have a minimally invasive procedure if they were aware that the intervention, albeit with fewer adverse effects, would be less effective than a tissue ablative intervention and would have a higher chance of requiring a second intervention.

Current UK clinical practice suggests a preference for oral medication using an alpha-blocker or 5-alpha-reductase inhibitor, alone or in combination, rather than the use of minimally invasive interventions. If oral medication fails to improve symptoms or if side effects develop, a tissue ablative intervention is offered. There is some evidence to suggest that the benefits offered by minimally invasive interventions are equivalent to those gained from oral medication[287–289] and so this could be a popular option for some men.

The economic model should be interpreted cautiously because of the assumptions and uncertainties that underpin it. The model suggests that TURP alone or repeated is amongst the more effective strategies although it is not cost-effective in the Markov model. The model reveals that other strategies are possibly less costly and slightly more effective. Should it be judged affordable then the results of the model suggest that a strategy of TUVP followed by up to two more TURPs (should a previous procedure fail) would be most likely to be considered cost-effective. At lower levels of willingness to pay, a policy of TUVP followed by HoLEP for failure might be worthwhile.

For the NHS, increased use of TUVP and/or holmium laser prostatectomy would lead to an increased requirement for training, which may be costly. Because of the limited number of surgeons currently providing these treatments it will take time to establish an adequate level of provision. It is unclear how long this will take as no evidence was found to indicate the speed at which surgeons may progress up the learning curves for these procedures. If interventions such as these are to be used as second-line procedures, it would be important that their use is limited to specialist centres only. However, in the absence of strong evidence in favour of newer methods, TURP remains clinically effective and cost-effective. The use of minimally invasive technologies in the NHS is not appropriate until a more effective and/or less costly technology is available.

Implications for future research

Research efforts in the management of clinical BPE should now be concentrated on the performance of higher-quality, more rigorous studies. As a minimum, these should be RCTs using predefined, ideally standardised, measures of outcome, and be multicentre to ensure sufficiently precise estimates of the various outcomes. Such trials should be protocol driven and a detailed protocol of how the project is to be conducted should be agreed before commencement of the study. The protocol should state the research objectives, reasons for the study, issues related to study recruitment (inclusion and exclusion criteria), information to be collected at entry to the study, interventions of interest and arrangements for follow-up. A crucial stage in the development of a study protocol is agreement on the definition of outcome measures of interest so that outcomes/complications reported in different collaborating centres share the same meaning. Although all outcome measures should be predefined, this is most important for specific outcome measures such as urinary incontinence,

urinary tract infection and failure of procedure. It is also essential that the reasons for reoperation be clearly stated, including when this decision is largely driven by patient choice. Future trials should also include direct measures of health state utilities.

In the context of the NHS and the patient, it is highly likely that choices based on strategies of management are more important than choices based on individual interventions. Areas in which further research would be important include:

1. For men who might currently be managed medically, a systematic review including modelling to determine how many years of medical treatment are necessary to offset the cost of treatment with a minimally invasive or ablative intervention in the first instance.
2. The true costs of the different interventions as a critical driver of economic evaluations.
3. Consensus work in partnership with governing bodies such as the British Association of Urological Surgeons to agree parameters for conducting future trials, such as standardising definitions and reporting of outcome measures.
4. For men judged to need ablative therapy, is there an alternative to TURP that is more effective, safe or cost-effective? A well-conducted head-to-head trial of treatment strategies – TUVP followed by either TURP or HoLEP versus HoLEP versus TURP × 2 – would be the most desirable to establish the gold standard. Such a trial should take prostate size into account and should also include direct measures of utility. Newer technologies could then be compared against this gold standard and, given the rapid developments in this area, a tracker trial approach may be appropriate.
5. Trials of different strategies aimed at improving outcomes and minimising adverse effects after TURP, particularly bleeding (the main serious adverse effect).

It should be stated clearly how data are to be collected and processed, what the primary and secondary outcome measures are and how statistical analysis will be conducted. The early involvement of trialists, statisticians and health economists is important to ensure that proposed trial designs and methods are appropriate, including sample size calculations. Consideration should be given to establishing a steering committee and a data monitoring committee to guide the conduct of the study.

In addition to any future RCT, a further area of research relevant to estimating cost-effectiveness, which might be performed as part of an RCT or as a parallel study, would consider in more detail how estimates of IPSS map on to estimates of utility and how utility, measured by a generic instrument, would change as IPSS changes. Such work would facilitate any modelling that may be required to extrapolate from the results of a future RCT.

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James N'Dow (Professor of Urology, clinical expert) led and co-ordinated all aspects of the project. Tania Lourenco (Research Fellow) reviewed the effectiveness of the technologies with the assistance of Angela Coutts (Research Assistant) and Susan Wong (Clinical Research Fellow), and wrote the executive summary with the assistance of James N'Dow. Nigel Armstrong (Research Fellow), with the assistance of Mark Deverill (Research Fellow) and Luke Vale (Senior Research Fellow), conducted the economic evaluation. Graham Mowatt (Research Fellow) commented on drafts of the report. Cynthia Fraser (Information Officer) developed and ran the search strategies and was responsible for obtaining papers and for reference management. Graeme MacLennan (Statistician) provided statistical support and advice. Robert Pickard (Senior Lecturer and Consultant Urological Surgeon, clinical expert), Samuel McClinton (Consultant Urological Surgeon, clinical expert), James N'Dow and Ghulam Nabi (Clinical Lecturer in Urology) wrote the background, developed the care pathways and provided clinical advice and critical comments. Adrian Grant (Director, methodology adviser) provided clinical and methodological advice and commented on drafts of the report. James N'Dow, Nigel Armstrong, Tania Lourenco, Luke Vale, Adrian Grant and Robert Pickard wrote the discussion and conclusions of the report.

References

1. Homma Y. Pressure-flow studies in benign prostatic hyperplasia: to do or not to do for the patient? *BJU Int* 2001;**87**:19–23.

2. Barry MJ, Fowler FJ, Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, *et al*. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;**148**:1549–57.

3. Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs FD, Fourcade R, *et al*. The prevalence of lower urinary tract symptoms in men and women in four centres. The UrEpik study. *BJU Int* 2003;**92**:409–14.

4. Fitzpatrick JM. The natural history of benign prostatic hyperplasia. *BJU Int* 2006;**97**:3–6.

5. Fong YK, Milani S, Djavan B. Natural history and clinical predictors of clinical progression in benign prostatic hyperplasia. *Curr Opin Urol* 2005;**15**:35–8.

6. Wasson JH, Reda DJ, Bruskewitz RC, Elinson J, Keller AM, Henderson WG. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. *N Engl J Med* 1995;**332**:75–9.

7. Jacobsen SJ, Girman CJ, Lieber MM. Natural history of benign prostatic hyperplasia. *Urology* 2001;**58**:5–16.

8. Sarma AV, Jacobsen SJ, Girman CJ, Jacobson DJ, Roberts RO, Rhodes T, *et al*. Concomitant longitudinal changes in frequency of and bother from lower urinary tract symptoms in community dwelling men. *J Urol* 2002;**168**:1446–52.

9. Roberts RO, Jacobsen SJ, Jacobson DJ, Rhodes T, Girman CJ, Lieber MM. Longitudinal changes in peak urinary flow rates in a community based cohort. *J Urol* 2000;**163**:107–13.

10. Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts RO, Rhodes T, Guess HA, *et al*. Natural history of prostatism: risk factors for acute urinary retention. *J Urol* 1997;**158**:481–7.

11. Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. *J Urol* 1984;**132**:474–9.

12. Guess HA. Epidemiology and natural history of benign prostatic hyperplasia. *Urol Clin North Am* 1995;**22**:247–61.

13. Wei JT, Calhoun EA, Jacobsen SJ. Benign prostatic hyperplasia. In Litwin MS, Saigal CS, editors. *Urologic diseases in America*. Washington DC National Institutes for Health, National Institute of Diabetes and Digestive and Kidney Diseases: US Government Publishing Office; 2004.

14. McConnell JD, Bruskewitz R, Walsh P, Andriole G, Lieber M, Holtgrewe HL, *et al*. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. Finasteride Long-Term Efficacy and Safety Study Group. *N Engl J Med* 1998;**338**:557–63.

15. United Nations. *World population prospects: the 2004 revision population database.* New York: Population Division of the Department of Economic & Social Affairs of the United Nations Secretariat; 2004. URL: http://esa.un.org/unpp. Accessed August 2006.

16. Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, *et al*. The prevalence of prostatism: a population-based survey of urinary symptoms. *J Urol* 1993;**150**:85–9.

17. Emberton M, Andriole GL, de la RJ, Djavan B, Hoefner K, Vela NR, *et al*. Benign prostatic hyperplasia: a progressive disease of aging men. *Urology* 2003;**61**:267–73.

18. Foley CL, Taylor C, Kirby RS. Counting the cost of treating benign prostatic hyperplasia. *BJU Int* 2004;**93**:250–2.

19. McConnell JD, Roehrborn CG, Bautista OM, Andriole GL, Jr, Dixon CM, Kusek JW, *et al*. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003;**349**:2387–98.

20. Barry MJ, Fowler FJ, Jr, Mulley AG, Jr, Henderson JV, Jr, Wennberg JE. Patient reactions to a program designed to facilitate patient participation in treatment decisions for benign prostatic hyperplasia. *Med Care* 1995;**33**:771–82.

21. AUA Practice Guidelines Committee. AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. *J Urol* 2003;170:530–47.

22. NHS Health and Social Care Information Centre. *Hospital episode statistics, 2006*. URL: www.hesonline.nhs.uk. Accessed August 2006.

23. Office for National Statistics. *United Kingdom Census 2001*. URL: www.statistics.gov.uk/census/. Accessed August 2006.

24. de la Rosette JJ, Alivizatos G, Madersbacher S, Rioja Sanz C, Nordling J, Emberton M, for the European Association of Urology. *Guidelines on benign prostatic hyperplasia*. URL: www.uroweb.nl/files/uploaded_files/guidelines/11%20BPH.pdf. Accessed March 2006.

25. Naspro R, Salonia A, Colombo R, Cestari A, Guazzoni G, Rigatti P, *et al*. Update of the minimally invasive therapies for benign prostatic hyperplasia. *Curr Opin Urol* 2005;**51**:49–53.

26. Rubenstein J, McVary KT. *Transurethral microwave thermotherapy of the prostate (TUMT)*. Emedicine, 2005. URL: www.emedicine.com/med/topic3070.htm. Accessed March 2006.

27. Boyle P, Robertson C, Vaughan ED, Fitzpatrick JM. A meta-analysis of trials of transurethral needle ablation for treating symptomatic benign prostatic hyperplasia.. *BJU Int* 2004;**94**:83–8.

28. Heaton JP. Radiofrequency thermal ablation of the prostate: the TUNA technique. *Tech Urol* 1995;**1**:3–10.

29. Muruve NA, Steinbecker K, Willard TB. *Transurethral needle ablation of the prostate (TUNA)*. Emedicine, 2005. URL: www.emedicine.com/med/topic3069.htm. Accessed March 2006.

30. Ogiste JS, Cooper K, Kaplan SA. Are stents still a useful therapy for benign prostatic hyperplasia? *Curr Opin Urol* 2003;**13**:51–7.

31. Madersbacher S, Marberger M. High-energy shockwaves and extracorporeal high-intensity focused ultrasound. *J Endourol* 2003;**17**:667–72.

32. Sullivan LD, McLoughlin MG, Goldenberg LG, Gleave ME, Marich KW. Early experience with high-intensity focused ultrasound for the treatment of benign prostatic hypertrophy. *Br J Urol* 1997;**79**:172–6.

33. Gelczer RK, Charboneau JW, Hussain S, Brown DL. Complications of percutaneous ethanol ablation. *J Ultrasound Med* 1998;**17**:531–3.

34. Chiang PH, Chuang YC, Huang CC, Chiang CP. Pilot study of transperineal injection of dehydrated ethanol in the treatment of prostatic obstruction. *Urology* 2003;**61**:797–801.

35. Levy DA, Cromeens DM, Evans R, Stephens LC, von Eschenbach AC, Pisters LL. Transrectal ultrasound-guided intraprostatic injection of absolute ethanol with and without carmustine: a feasibility study in the canine model. *Urology* 1999;**53**:1245–51.

36. Mutaguchi K, Matsubara A, Kajiwara M, Hanada M, Mizoguchi H, Ohara S, *et al*. Transurethral ethanol injection for prostatic obstruction: an excellent treatment strategy for persistent urinary retention. *Urology* 2006;**68**:307–11.

37. Goya N, Ishikawa N, Ito F, Kobayashi C, Tomizawa Y, Toma H. Transurethral ethanol injection therapy for prostatic hyperplasia: 3-year results. *J Urol* 2004;**172**:1017–20.

38. Muschter R. Conductive heat: hot water-induced thermotherapy for ablation of prostatic tissue. *J Endourol* 2003;**17**:609–16.

39. Muschter R, Schorsch I, Danielli L, Russel C, Timoney A, Yachia D, *et al*. Transurethral water-induced thermotherapy for the treatment of benign prostatic hyperplasia: a prospective multicenter clinical trial. *J Urol* 2000;**164**:9.

40. Brosman SA. *Interstitial laser coagulation of the prostate*. Emedicine, 2006. URL: www.emedicine.com/med/topic3033.htm. Accessed August 2006.

41. *Prostate management*. Medcompare. The buyer's guide for medical professionals, 2006. URL: www.medcompare.com/. Accessed June 2006.

42. Emberton M, Neal DE, Black N, Harrison M, Fordham M, McBrien MP, *et al*. The National Prostatectomy Audit: the clinical management of patients during hospital admission. *Br J Urol* 1995;**75**:301–16.

43. Reich O, Gratzke C, Stief CG. Techniques and long-term results of surgical procedures for BPH. *Eur Urol* 2006;**49**:970–8.

44. Lynch M, Anson K. Time to rebrand transurethral resection of the prostate? *Curr Opin Urol* 2006;**16**:20–4.

45. *NHS reference costs.* NHS trusts elective in-patient HRG data. London: UK Department of Health; 2005. URL: www.dh.gov.uk/PolicyAndGuidance/OrganisationPolicy/FinanceAndPlanning/NHSReferenceCosts/fs/en. Accessed August 2006.

46. Riehmann M, Bruskewitz R. Transurethral incision of the prostate and bladder neck. *J Androl* 1991;**12**:415–22.

47. Yang Q, Peters TJ, Donovan JL, Wilt TJ, Abrams P. Transurethral incision compared with transurethral resection of the prostate for bladder outlet obstruction: a systematic review and meta-analysis of randomized controlled trials. *J Urol* 2001;**165**:1526–32.

48. Kaplan SA, Te AE. Transurethral electrovaporization of the prostate: a novel method for treating men with benign prostatic hyperplasia. *Urology* 1995;**45**:566–72.

49. Wilson LC, Gilling PJ. From coagulation to enucleation: the use of lasers in surgery for benign prostatic hyperplasia. *Nat Clin Pract Urol* 2005;**2**:443–8.

50. Daughtry JD, Rodan BA. Transurethral laser prostatectomy: a comparison of contact tip mode and lateral firing free beam mode. *J Clin Laser Med Surg* 1993;**11**:21–8.

51. Kuntz RM. Current role of lasers in the treatment of benign prostatic hyperplasia (BPH). *Eur Urol* 2006;**49**:961–9.

52. Te AE. The development of laser prostatectomy. *BJU Int* 2004;**93**:262–5.

53. Gilling PJ, Fraundorfer MR. Holmium laser prostatectomy: a technique in evolution. *Curr Opin Urol* 1998;**8**:11–15.

54. Sandhu JS, Ng C, Vanderbrink BA, Egan C, Kaplan SA, Te AE. High-power potassium-titanyl-phosphate photoselective laser vaporization of prostate for treatment of benign prostatic hyperplasia in men with large prostates. *Urology* 2004;**64**:1155–9.

55. Kaplan SA, Laor E, Fatal M, Te AE. Transurethral resection of the prostate versus transurethral electrovaporization of the prostate: a blinded, prospective comparative study with 1-year followup. *J Urol* 1998;**159**:454–8.

56. Tewari A, Narayan P. Electrovaporization of the prostate. *Br J Urol* 1996;**78**:667–76.

57. Fowler C, McAllister W, Plail R, Karim O, Yang Q. Randomised evaluation of alternative electrosurgical modalities to treat bladder outflow obstruction in men with benign prostatic hyperplasia. *Health Technol Assess* 2005;**9**:1–30.

58. Botto H, Lebret T, Barre P, Orsoni JL, Herve JM, Lugagne PM. Electrovaporization of the prostate with the Gyrus device. *J Endourol* 2001;**15**:313–16.

59. Smith D, Khoubehi B, Patel A. Bipolar electrosurgery for benign prostatic hyperplasia: transurethral electrovaporization and resection of the prostate. *Curr Opin Urol* 2005;**15**:95–100.

60. Sandhu JS, Ng AS, Gonzalez RR, Kaplan SA, Te AE. Photoselective laser vaporization prostatectomy in men receiving anticoagulants. *J Endourol* 2005;**19**:1196–8.

61. Kuo RL, Paterson RF, Kim SC, Siqueira TM, Jr, Elhilali MM, Lingeman JE. Holmium laser enucleation of the prostate (HoLEP): a technical update. *World J Surg Oncol* 2003;**1**:6.

62. Aho TF, Gilling PJ, Kennett KM, Westenberg AM, Fraundorfer MR, Frampton CM. Holmium laser bladder neck incision versus holmium enucleation of the prostate as outpatient procedures for prostates less than 40 grams: a randomized trial. *J Urol* 2005;**174**:210–14.

63. Gilling PJ, Kennett KM, Fraundorfer MR. Holmium laser resection v transurethral resection of the prostate: results of a randomized trial with 2 years of follow-up. *J Endourol* 2000;**14**:757–60.

64. Kuntz RM, Ahyai S, Lehrich K, Fayad A. Transurethral holmium laser enucleation of the prostate versus transurethral electrocautery resection of the prostate: a randomized prospective trial in 200 patients. *J Urol* 2004;**172**:1012–16.

65. de Sio M, Autorino R, Quarto G, Damiano R, Perdona S, di Lorenzo G, *et al*. Gyrus bipolar versus standard monopolar transurethral resection of the prostate: a randomized prospective trial. *Urology* 2006;**67**:69–72.

66. Eaton AC, Francis RN. The provision of transurethral prostatectomy on a day-case basis using bipolar plasma kinetic technology. *BJU Int* 2002;**89**:534–7.

67. Starkman JS, Santucci RA. Comparison of bipolar transurethral resection of the prostate with standard transurethral prostatectomy: shorter stay, earlier catheter removal and fewer complications. *BJU Int* 2005;**95**:69–71.

68. Talic RF, El Tiraifi A, El Faqih SR, Hassan SH, Attassi RA, Abdel-Halim RE. Prospective randomized study of transurethral vaporization resection of the prostate using the thick loop and

standard transurethral prostatectomy. *Urology* 2000;**55**:886–90.

69. Gilling PJ, Mackey M, Cresswell M, Kennett K, Kabalin JN, Fraundorfer MR. Holmium laser versus transurethral resection of the prostate: a randomized prospective trial with 1-year follow-up. *J Urol* 1999;**162**:1640–4.

70. Hon NHY, Brathwaite D, Hussain Z, Ghiblawi S, Brace H, Hayne D, *et al*. A prospective, randomized trial comparing conventional transurethral prostate resection with plasmakinetic vaporization of the prostate: physiological changes, early complications and long-term follow-up. *J Urol* 2006;**176**:205–9.

71. Kuntz RM, Lehrich K. Transurethral holmium laser enucleation versus transvesical open enucleation for prostate adenoma greater than 100 gm: a randomized prospective trial of 120 patients. *J Urol* 2002;**168**:1465–9.

72. Kabalin JN, Gilling PJ, Fraundorfer MR. Application of the holmium:YAG laser for prostatectomy. *J Clin Laser Med Surg* 1998;**16**:21–7.

73. MacDonald D, McNicholas TA. Drug treatments for lower urinary tract symptoms secondary to bladder outflow obstruction: focus on quality of life. *Drugs* 2003;**63**:1947–62.

74. DiSantostefano RL, Biddle AK, Lavelle JP. The long-term cost-effectiveness of treatments for benign prostatic hyperplasia. *Pharmacoeconomics* 2006;**24**:171–91.

75. Drummond MF, Sculpher M, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press; 1997.

76. Briggs A. Handling uncertainty in economic evaluations and presenting the results. In McGuire DM, McGuire A, editors. *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press; 2001. p. 172–214.

77. Ades AE, Lu G, Claxton K. Expected value of sample information calculations in medical decision modeling. *Med Decis Making* 2004;**24**:207–27.

78. Ackerman SJ, Rein AL, Blute M, Beusterien K, Sullivan EM, Tanio CP, *et al*. Cost-effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: I: Methods. *Urology* 2000;**56**:972–80.

79. Blute M, Ackerman SJ, Rein AL, Beusterien K, Sullivan EM, Tanio CP, *et al*. Cost-effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: II: Results. *Urology* 2000;**56**:981–7.

80. Manyak MJ, Ackerman SJ, Blute ML, Rein AL, Buesterien K, Sullivan EM, *et al*. Cost-effectiveness of treatment for benign prostatic hyperplasia: an economic model for comparison of medical, minimally invasive, and surgical therapy. *J Endourol* 2002;**16**:51–6.

81. DiSantostefano RL, Biddle AK, Lavelle JP. An evaluation of the economic costs and patient-related consequences of treatments for benign prostatic hyperplasia. *BJU Int* 2006;**97**:1007–16.

82. Howard K, Wortley S. *Transurethral needle ablation (TUNA) for the treatment of benign prostatic hyperplasia. MSAC application 1014*. Medical Services Advisory Committee, 2002. URL: www.msac.gov.au/internet/msac/publishing.nsf/Content/1014–1. Accessed July 2005.

83. Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998;**13**:397–409.

84. Agency for Health Care Policy and Research. *Benign prostatic hyperplasia: diagnosis and treatment*. Clinical Practice Guideline No. 8. Agency for Health Care Policy and Research, 1994. URL: www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat6.chapter.17571. Accessed August 2005.

85. American Urological Association. *Guideline on the management of benign prostatic hyperplasia (BPH)*. American Urological Association, 2003. URL: www.auanet.org/guidelines/bph.cfm. Accessed August 2005.

86. Francisca EA, d'Ancona FC, Meuleman EJ, Debruyne FM, de la Rosette JJ. Sexual function following high energy microwave thermotherapy: results of a randomized controlled study comparing transurethral microwave thermotherapy to transurethral prostatic resection. *J Urol* 1999;**161**:486–90.

87. Madersbacher S, Lackner J, Brossner C, Rohlich M, Stancik I, Willinger M, *et al*. Reoperation, myocardial infarction and mortality after transurethral and open prostatectomy: a nation-wide, long-term analysis of 23,123 cases. *Eur Urol* 2005;**47**:499–504.

88. NHS Centre for Reviews and Dissemination. *Undertaking systematic reviews of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews*. CRD Report No 4. University of York: Centre for Reviews and Dissemination; 2001.

89. Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Bouter LM, *et al*. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews

developed by Delphi consensus. *J Clin Epidemiol* 1998;**51**:1235–41.

90. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;**52**:377–84.

91. Chapple CR, Rosario DJ, Wasserfallen M, Woo HH. A randomised study of the urolume stent vs prostatic surgery. *J Urol* 1995;**153**:436A.

92. Gilling PJ, Kennett K, Aho T, Westenberg A, Fraundorfer M. Holmium bladder neck incision vs holmium laser enucleation of the prostate (HOLEP) as outpatient clinic procedures for small prostate glands (<40 g): a randomised trial with one year follow-up. *J Urol* 2004;**171**:410.

93. Ho H, Tatt K, Cheng C. A prospective randomized controlled trial comparing bipolar transurethral resection in saline (TURIS) system and conventional monopolar transurethral resection of prostate in men with benign prostate hyperplasia: a 1 year's clinical efficacy and safety. *J Endourol* 2005;**19**:A47.

94. Chiou RK, Binard JE, Ebersole ME, Horan JJ, Chiou YK, Lynch B. Randomized comparison of balloon dilation and transurethral incision for treatment of symptomatic benign prostatic hyperplasia. *J Endourol* 1994;**8**:221–4.

95. D'Addessi A, Porreca A, Foschi N, Racioppi M. Thick loop prostatectomy in the endoscopic treatment of benign prostatic hyperplasia: results of a prospective randomised study. *Urol Int* 2005;**74**:114–17.

96. Holmes M, Cox J, Stewart J, King D, Bary P, Wright W. Thick vs thin loop transurethral resection of the prostate: a double-blind prospective trial of early morbidity. *BJU Int* 2002;**89**:197–201.

97. Leskinen MJ, Kilponen A, Lukkarinen O, Tammela TL. Transurethral needle ablation for the treatment of chronic pelvic pain syndrome (category III prostatitis): a randomized, sham-controlled study. *Urology* 2002;**60**:300–4.

98. Talic RF, El Tiraifi A, El Faqih SR, Abdel-Halim RE. A prospective randomized study of the thick loop and standard wire-loop in transurethral prostatectomy: one year follow up. *J Endourol* 2000;**14**:A36.

99. Tsukada O, Murakami M, Kosuge T, Yokoyama H. Treatment of benign prostatic hyperplasia using transurethral microwave thermotherapy and dilatation with double-balloon catheter. *J Endourol* 2005;**19**:1016–20.

100. Yeni E, Unal D, Verit A, Gulum M. Minimal transurethral prostatectomy plus bladder neck incision versus standard transurethral prostatectomy in patients with benign prostatic hyperplasia: a randomised prospective study. *Urol Int* 2002;**69**:283–6.

101. Hansen BJ, Flyger H, Mortensen S, Mensink HJ, Meyhoff HH. Symptomatic outcome of transurethral prostatectomy, alpha-blockade and placebo in the treatment of benign prostatic hyperplasia. Evaluation of treatment with the Danish Prostatic Symptom Score (DAN-PSS-1) system. The ALFECH Study Group. *Scand J Urol Nephrol* 1996;**30**:103–7.

102. Petas A, Isotalo T, Talja M, Tammela TL, Valimaa T, Tormala P. A randomised study to evaluate the efficacy of a biodegradable stent in the prevention of postoperative urinary retention after interstitial laser coagulation of the prostate. *Scand J Urol Nephrol* 2000;**34**:262–6.

103. Roehrborn CG, Rhee EY, Miller SD, Brawer MK, Heron SP, Ruckle HC, *et al*. Initial results of a randomized multi-center trial comparing the efficacy and safety of Indigo Optima laser treatment with tamsulosin in men with LUTS and BPH. *J Urol* 2005;**173**:424.

104. Yamamoto M, Hibi H, Miyake K. A comparison of transurethral resection of the prostate and medical treatment for the patient with moderate symptoms of benign prostatic hyperplasia. *Nagoya J Med Sci* 1996;**59**:11–16.

105. A comparison of quality of life with patient reported symptoms and objective findings in men with benign prostatic hyperplasia. The Department of Veterans Affairs Cooperative Study of transurethral resection for benign prostatic hyperplasia. *J Urol* 1993;**150**:1696–700.

106. Plante M. A safety comparison of a randomized mutli-centre study evaluating transurethral ethanol ablation of the prostate (TEAP) for the treatment of benign prostatic hyperplasia (BPH). *Eur Urol Suppl* 2004;**3**:143.

107. Abbou C-C, Colombel M, Payan C, Viens-Bitker C, Richard F, Boccon L, *et al*. Transrectal and transurethral hyperthermia versus sham to treat benign prostatic hyperplasia: a double blind, randomized, multicentric study. *J Urol* 1994;**151**:418A.

108. Billebaud T, Mechali P, Astier L, Monneins F, Savatovsky I, Coloby P. Transurethral microwave hyperthermia for benign prostatic hyperplasia: is it effective? Results of a multicentric randomized prospective study versus placebo with six month follow-up. *J Urol* 1994;**151**:417A.

109. Brookes S, Peters T, Campbell R, Featherstone K, Neal D, Abrams P, *et al*. Including a 'no active intervention' arm in surgical trials is possible: evidence from the CLasP randomised trial. *J Health Serv Res Policy* 2003;**8**:209–14.

110. Çetinkaya M, Ozturk B, Akdemir O, Aki FT. A comparison of fluid absorption during transurethral resection and transurethral vaporization for benign prostatic hyperplasia. *BJU Int* 2000;**86**:820–3.

111. de la Rosette JJ, Floratos DL, Severens JL, Laguna MP, Kiemeney LA, Debruyne FM. Cost-consequences analysis of TUMT compared to TURP. Results of a randomized study. *J Urol* 2001;**165**:292.

112. Holtgrewe HL. An American Urological Association prospective, randomized clinical trial in the treatment of benign prostatic hyperplasia. *Cancer* 1992;**70**:351–4.

113. Kuntz RM, Lehrich K, Fayad A. Transurethral holmium laser enucleation of the prostate (HoLEP) compared to traditional transurethral resection of the prostate (TURP) for prostates smaller than 100 grams: a randomized prospective clinical study. *J Endourol* 2001;**15**:A41.

114. Lawrence WT. Ablation of the prostate by laser (ELAP). *Journal d' Urologie* 1993;**99**:351.

115. Norby B, Nielsen HV, Frimodt-Moller PC. Cost-effectiveness of new treatments for benign prostatic hyperplasia: results of a randomized trial comparing the short-term cost-effectiveness of transurethral interstitial laser coagulation of the prostate, transurethral microwave thermotherapy and standard transurethral resection or incision of the prostate. *Scand J Urol Nephrol* 2002;**36**:286–95.

116. Patel A, Fuchs GJ, Gutierrez-Aceves J, Ryan TP. A prospectively randomized study of energy utilization during transurethral electrosurgical resection (TURP) and electro-vaporization (TUEVAP). *J Endourol* 1996;**10**:S82.

117. Patel A, Fuchs GJ, Gutierrez-Aceves J. A pilot study of energy utilization patterns during different transurethral electrosurgical treatments of the prostate. *Urology* 1997;**50**:138–41.

118. Patankar SB, Dobhada SH. Superpulse bipolar prostate resection vs conventional TURP: a randomized prospective trial with 3 months follow-up – and Indian experience. *J Endourol* 2004;**18**:A77.

119. Eaton AC, de Silva B, Duncan NH, Francis RN. A randomised prospective study comparing the performance of the 4mm plasma kinetic loop against the standard monopolar TURP in prostates 40–100 gm size. *J Urol* 2004;**171**:398.

120. Lloyd SN. A multicentre comparative study of the Gyrus plasmakinetic bipolar electrosurgical system and conventional monopolar loop TURP in BPH. *BJU Int* 2002;**90**:13.

121. Tuhkanen K, Heino A, Aaltoma S, Ala-Opas M. Sexual function of LUTS patients before and after neodymium laser prostatectomy and transurethral resection of prostate. A prospective, randomized trial. *Urol Int* 2004;**73**:137–42.

122. Patel A, Fuchs GJ, Gutierrez-Aceves J, Andrade-Perez F. Completeness and efficiency of prostate tissue removal: loop resection compared with a new operative technique of transurethral electrovaporization. *BJU Int* 1999;**84**:43–9.

123. Costello AJ, Crowe HR, Jackson T, Street A. A randomised single institution study comparing laser prostatectomy and transurethral resection of the prostate. *Ann Acad Med* 1995;**24**:700–4.

124. Ahmed M, Bell T, Lawrence WT, Ward JP, Watson GM. Transurethral microwave thermotherapy (Prostatron version 2.5) compared with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: a randomized, controlled, parallel study. *Br J Urol* 1997;**79**:181–5.

125. Bdesha AS, Bunce CJ, Snell ME, Witherow RO. Sham controlled trial of transurethral microwave therapy with subsequent treatment of the control-group. *J Urol* 1994;**152**:453–8.

126. Blute ML, Patterson DE, Segura JW, Tomera KM, Hellerstein DK. Transurethral microwave thermotherapy v sham treatment: double-blind randomized study. *J Endourol* 1996;**10**:565–73.

127. Carter A, Sells H, Speakman M, Ewings P, MacDonagh R, O'Boyle P. A prospective randomized controlled trial of hybrid laser treatment or transurethral resection of the prostate, with a 1-year follow-up. *BJU Int* 1999;**83**:254–9.

128. Erdağı U, Akman RY, Sargin SY, Yazicioglu A. Transurethral electrovaporization of the prostate versus transurethral resection of the prostate: a prospective randomized study. *Arch Ital Urol Androl* 1999;**71**:125–30.

129. Hammadeh MY, Madaan S, Hines J, Philp T. 5-year outcome of a prospective randomized trial to compare transurethral electrovaporization of the prostate and standard transurethral resection. *Urology* 2003;**61**:1166–71.

130. Kursh ED, Concepcion R, Chan S, Hudson P, Ratner M, Eyre R. Interstitial laser coagulation versus transurethral prostate resection for treating benign prostatic obstruction: a randomized trial with 2-year follow-up. *Urology* 2003;**61**:573–8.

131. Liedberg F, Adell L, Hagberg G, Palmqvist IB. Interstitial laser coagulation versus transurethral resection of the prostate for benign prostatic enlargement – a prospective randomized study. *Scand J Urol Nephrol* 2003;**37**:494–7.

132. Liu CK, Lee WK, Ko MC, Chiang HS, Wan KS. Transurethral electrovapor resection versus standard transurethral resection treatment for a large prostate: a 2-year follow-up study conducted in Taiwan. *Urol Int* 2006;**76**:144–9.

133. Ogden C, Reddy P, Johnson H, Carter S. Sham vs TUMT: a randomized study with cross over. *J Urol* 1993;**149**(Suppl 4):250A.

134. Wilson LC, Gilling P, Williams A, Kennett KM, Frampton CM, Westenberg AM, *et al*. A randomised trial comparing holmium laser enucleation versus transurethral resection in the treatment of prostates larger than 40 grams: results at 2 years. *Eur Urol* 2006;**50**:569–73.

135. Christensen MM, Aagaard J, Madsen PO. Transurethral resection versus transurethral incision of the prostate. A prospective randomized study. *Urol Clin North Am* 1990;**17**:621–30.

136. Donovan JL, Peters TJ, Neal DE, Brookes ST, Gujral S, Chacko KN, *et al*. A randomized trial comparing transurethral resection of the prostate, laser therapy and conservative treatment of men with symptoms associated with benign prostatic enlargement: the CLasP study. *J Urol* 2000;**164**:65–70.

137. Dunsmuir WD, McFarlane JP, Tan A, Dowling C, Downie J, Kourambas J, *et al*. Gyrus bipolar electrovaporization vs transurethral resection of the prostate: a randomized prospective single-blind trial with 1 y follow-up. *Prostate Cancer Prostatic Dis* 2003;**6**:182–6.

138. Gallucci M, Puppo P, Perachino M, Fortunato P, Muto G, Breda G, *et al*. Transurethral electrovaporization of the prostate vs. transurethral resection. Results of a multicentric, randomized clinical study on 150 patients. *Eur Urol* 1998;**33**:359–64.

139. Gujral S, Abrams P, Donovan JL, Neal DE, Brookes ST, Chacko KN, *et al*. A prospective randomized trial comparing transurethral resection of the prostate and laser therapy in men with chronic urinary retention: the CLasP study. *J Urol* 2000;**164**:59–64.

140. Patel A, Fuchs GJ, Gutierrez-Aceves J, Ryan TP. Prostate heating patterns comparing electrosurgical transurethral resection and vaporization: a prospective randomized study. *J Urol* 1997;**157**:169–72.

141. Bouchier-Hayes DM, Anderson P, Van Appledorn S, Bugeja P, Costello AJ. KTP laser versus transurethral resection: early results of a randomized trial. *J Endourol* 2006;**20**:580–5.

142. Ekengren J, Haendler L, Hahn RG. Clinical outcome 1 year after transurethral vaporization and resection of the prostate. *Urology* 2000;**55**:231–5.

143. Abbou C-C, Payan C, Viens-Bitker C, Richard F, Boccon-Gibod L, Jardin A, *et al*. Transrectal and transurethral hyperthermia versus sham treatment in benign prostatic hyperplasia: a double-blind randomized multicentre clinical trial. *Br J Urol* 1995;**76**:619–24.

144. Hill B, Belville W, Bruskewitz R, Issa M, Perez-Marrero R, Roehrborn C, *et al*. Transurethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. *J Urol* 2004;**171**:2336–40.

145. McAllister WJ, Absalom MJ, Mir K, Shivde S, Anson K, Kirby RS, *et al*. Does endoscopic laser ablation of the prostate stand the test of time? Five-year results from a multicentre randomized controlled trial of endoscopic laser ablation against transurethral resection of the prostate. *BJU Int* 2000;**85**:437–9.

146. Shingleton WB, Farabaugh P, May W. Three-year follow-up of laser prostatectomy versus transurethral resection of the prostate in men with benign prostatic hyperplasia. *Urology* 2002;**60**:305–8.

147. Singh H, Desai MR, Shrivastav P, Vani K. Bipolar versus monopolar transurethral resection of prostate: randomized controlled study. *J Endourol* 2005;**19:**333–8.

148. Zorn BH, Bauer JJ, Ruiz HE, Thrasher JB. Randomized trial of safety and efficacy of transurethral resection of the prostate using contact laser versus electrocautery. *Tech Urol* 1999;**5**:198–201.

149. Rodrigo Aliaga M, Valls Blasco F, Jimenez Cruz JF. Lasers as an alternative to the endoscopic surgery in BPH. *Actas Urol Esp* 1998;**22**:17–22.

150. Kim JY, Moon KH, Yoon CJ, Park TC. Bipolar transurethral resection of the prostate: a comparative study with monopolar transurethral resection. *Korean J Urol* 2006;**47**:493–7.

151. Kim TS, Choi S, Rhew HY, Ahn JH, Jang JH, Cho MH. Comparative study on the treatment outcome and safety of TURP, ILC, TUNA and TEAP for patients with benign prostatic hyperplasia. *Korean J Urol* 2006;**47**:13–19.

152. Riehmann M, Knes JM, Heisey D, Madsen PO, Bruskewitz RC. Transurethral resection versus incision of the prostate: a randomized, prospective study. *Urology* 1995;**45**:768–75.

153. Tuhkanen K, Heino A, Aaltomaa S, Ala-Opas M. Long-term results of contact laser versus transurethral resection of the prostate in the treatment of benign prostatic hyperplasia with small or moderately enlarged prostates. *Scand J Urol Nephrol* 2003;**37**:487–93.

154. Chacko KN, Donovan JL, Abrams P, Peters TJ, Brookes ST, Thorpe AC, *et al*. Transurethral prostatic resection or laser therapy for men with acute urinary retention: the CLasP randomized trial. *J Urol* 2001;**166**:166–70.

155. Fung BT, Li SK, Yu CF, Lau BE, Hou SS. Prospective randomized controlled trial comparing plasmakinetic vaporesection and conventional transurethral resection of the prostate. *Asian J Surg* 2005;**28**:24–8.

156. Gotoh M, Okamura K, Hattori R, Nishiyama N, Kobayashi H, Tanaka K, *et al*. A randomized comparative study of the Bandloop versus the standard loop for transurethral resection of the prostate. *J Urol* 1999;**162**:1645–7.

157. Hellström P, Lukkarinen O, Kontturi M. Bladder neck incision or transurethral electroresection for the treatment of urinary obstruction caused by a small benign prostate? A randomized urodynamic study. *Scand J Urol Nephrol* 1986;**20**:187–92.

158. Küpeli S, Baltaci S, Soygur T, Aytac S, Yilmaz E, Budak M. A prospective randomized study of transurethral resection of the prostate and transurethral vaporization of the prostate as a therapeutic alternative in the management of men with BPH. *Eur Urol* 1998;**34**:15–18.

159. Larson TR, Blute ML, Bruskewitz RC, Mayer RD, Ugarte RR, Utz WJ. A high-efficiency microwave thermoablation system for the treatment of benign prostatic hyperplasia: results of a randomized, sham-controlled, prospective, double-blind, multicenter clinical trial. *Urology* 1998;**51**:731–42.

160. Nawrocki JD, Bell TJ, Lawrence WT, Ward JP. A randomized controlled trial of transurethral microwave thermotherapy. *Br J Urol* 1997;**79**:389–93.

161. Seckiner I, Yesilli C, Akduman B, Altan K, Mungan NA. A prospective randomized study for comparing bipolar plasmakinetic resection of the prostate with standard TURP. *Urol Int* 2006;**76**:139–43.

162. Nathan MS, Wickham JEA. TVP: a cheaper and effective alternative to TURP. *Minim Invasive Ther Allied Technol* 1996;**5**:292–6.

163. Cowles RS, III, Kabalin JN, Childs S, Lepor H, Dixon C, Stein B, *et al*. A prospective randomized comparison of transurethral resection to visual laser ablation of the prostate for the treatment of benign prostatic hyperplasia. *Urology* 1995;**46**:155–60.

164. Keoghane SR, Lawrence KC, Gray AM, Doll HA, Hancock AM, Turner K, *et al*. A double-blind randomized controlled trial and economic evaluation of transurethral resection vs contact laser vaporization for benign prostatic enlargement: a 3-year follow-up. *BJU Int* 2000;**85**:74–8.

165. Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, Schain M, *et al*. Feedback microwave thermotherapy versus TURP for clinical BPH – a randomized controlled multicenter study. *Urology* 2002;**60**:292–9.

166. d'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, de la Rosette JJ. Transurethral resection of the prostate vs high-energy thermotherapy of the prostate in patients with benign prostatic hyperplasia: long-term results. *Br J Urol* 1998;**81**:259–64.

167. Dahlstrand C, Geirsson G, Fall M, Pettersson S. Transurethral microwave thermotherapy versus transurethral resection for benign prostatic hyperplasia: preliminary results of a randomized study. *Eur Urol* 1993;**23**:292–8.

168. Dahlstrand C, Walden M, Geirsson G, Pettersson S. Transurethral microwave thermotherapy versus transurethral resection for symptomatic benign prostatic obstruction: a prospective randomized study with a 2-year follow-up. *Br J Urol* 1995;**76**:614–8.

169. de la Rosette JJ, Floratos DL, Severens JL, Kiemeney LA, Debruyne FM, Pilar LM. Transurethral resection vs microwave thermotherapy of the prostate: a cost-consequences analysis. *BJU Int* 2003;**92**:713–8.

170. Albala DM, Fulmer BR, Turk TM, Koleski F, Andriole G, Davis BE, *et al*. Office-based transurethral microwave thermotherapy using the TherMatrx TMx-2000. *J Endourol* 2002;**16**:57–61.

171. Brehmer M, Wiksell H, Kinn A. Sham treatment compared with 30 or 60 min of thermotherapy for

benign prostatic hyperplasia: a randomized study. *BJU Int* 1999;**84**:292–6.

172. de Wildt MJ, Hubregtse M, Ogden C, Carter SS, Debruyne FM, de la Rosette JJ. A 12-month study of the placebo effect in transurethral microwave thermotherapy. *Br J Urol* 1996;**77**:221–7.

173. Trachtenberg J, Roehrborn CG. Updated results of a randomized, double-blind, multicenter sham-controlled trial of microwave thermotherapy with the Dornier Urowave in patients with symptomatic benign prostatic hyperplasia. Urowave Investigators Group. *World J Urol* 1998;**16**:102–8.

174. Zerbib M, Steg A, Conquy S, Debre B. Hyperhermia: a randomized prospective study applying hyperthermia or a sham procedure in obstructive benign hyperplasia of the prostate. *Prog Clin Biol Res* 1994;**386**:439–48.

175. Cimentepe E, Unsal A, Saglam R. Randomized clinical trial comparing transurethral needle ablation with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: results at 18 months. *J Endourol* 2003;**17**:103–7.

176. Hindley RG, Mostafid AH, Brierly RD, Harrison NW, Thomas PJ, Fletcher MS. The 2-year symptomatic and urodynamic results of a prospective randomized trial of interstitial radiofrequency therapy vs transurethral resection of the prostate. *BJU Int* 2001;**88**:217–20.

177. Kabalin JN, Gill HS, Bite G, Wolfe V. Comparative study of laser versus electrocautery prostatic resection: 18-month followup with complex urodynamic assessment. *J Urol* 1995;**153**:94–7.

178. Mårtenson AC, de la Rosette JJMC. Interstitial laser coagulation in the treatment of benign prostatic hyperplasia using a diode laser system: results of an evolving technology. *Prostate Cancer Prostatic Dis* 1999;**2**:148–54.

179. Suvakovic N, Hindmarsh JR. A step towards day case prostatectomy. *Br J Urol* 1996;**77**:212–14.

180. Dørflinger T, Jensen FS, Krarup T, Walter S. Transurethral prostatectomy compared with incision of the prostate in the treatment of prostatism caused by small benign prostate glands. *Scand J Urol Nephrol* 1992;**26**:333–8.

181. Jahnson S, Dalen M, Gustavsson G, Pedersen J. Transurethral incision versus resection of the prostate for small to medium benign prostatic hyperplasia. *Br J Urol* 1998;**81**:276–81.

182. Li MK, Ng AS. Bladder neck resection and transurethral resection of the prostate: a randomized prospective trial. *J Urol* 1987;**138**:807–9.

183. Nielsen HO. Transurethral prostatotomy versus transurethral prostatectomy in benign prostatic hypertrophy. A prospective randomised study. *Br J Urol* 1988;**61**:435–8.

184. Saporta L, Aridogan IA, Erlich N, Yachia D. Objective and subjective comparison of transurethral resection, transurethral incision and balloon dilatation of the prostate. A prospective study. *Eur Urol* 1996;**29**:439–45.

185. Soonawalla PF, Pardanani DS. Transurethral incision versus transurethral resection of the prostate. A subjective and objective analysis. *Br J Urol* 1992;**70**:174–7.

186. Tkocz M, Prajsner A. Comparison of long-term results of transurethral incision of the prostate with transurethral resection of the prostate, in patients with benign prostatic hypertrophy. *Neurourol Urodyn* 2002;**21**:112–16.

187. Gupta N, Sivaramakrishna, Kumar R, Dogra PN, Seth A. Comparison of standard transurethral resection, transurethral vapour resection and holmium laser enucleation of the prostate for managing benign prostatic hyperplasia of >40 g. *BJU Int* 2006;**97**:85–9.

188. Montorsi F, Naspro R, Salonia A, Suardi N, Briganti A, Zanoni M, *et al*. Holmium laser enucleation versus transurethral resection of the prostate: results from a 2-center, prospective, randomized trial in patients with obstructive benign prostatic hyperplasia. *J Urol* 2004;**172**:1926–9.

189. Westenberg A, Gilling P, Kennett K, Frampton C, Fraundorfer M. Holmium laser resection of the prostate versus transurethral resection of the prostate: results of a randomized trial with 4-year minimum long-term followup. *J Urol* 2004;**172**:616–19.

190. Mottet N, Anidjar M, Bourdon O, Louis JF, Teillac P, Costa P, *et al*. Randomized comparison of transurethral electroresection and holmium: YAG laser vaporization for symptomatic benign prostatic hyperplasia. *J Endourol* 1999;**13**:127–30.

191. Tuhkanen K, Heino A, Ala-Opas M. Two-year follow-up results of a prospective randomized trial comparing hybrid laser prostatectomy with TURP in the treatment of big benign prostates. *Scand J Urol Nephrol* 2001;**35**:200–4.

192. Sengör F, Kose O, Yucebas E, Beysel M, Erdogan K, Narter F. A comparative study of laser ablation and transurethral electroresection for benign prostatic

hyperplasia: results of a 6-month follow-up. *Br J Urol* 1996;**78**:398–400.

193. van Melick HH, van Venrooij GE, Boon TA. Long-term follow-up after transurethral resection of the prostate, contact laser prostatectomy, and electrovaporization. *Urology* 2003;**62**:1029–34.

194. Nuhoğlu B, Ayyildiz A, Karaguzel E, Cebeci O, Germiyanoglu C. Plasmakinetic prostate resection in the treatment of benign prostate hyperplasia: results of 1-year follow up. *Int J Urol* 2006;**13**:21–4.

195. Tefekli A, Muslumanoglu AY, Baykal M, Binbay M, Tas A, Altunrende F. A hybrid technique using bipolar energy in transurethral prostate surgery: a prospective, randomized comparison. *J Urol* 2005;**174**:1339–43.

196. Çetinkaya M, Ulusoy E, Adsan O, Saglam H, Ozturk B, Basay S. Comparative early results of transurethral electroresection and transurethral electrovaporization in benign prostatic hyperplasia. *Br J Urol* 1996;**78**:901–3.

197. Küpeli B, Yalcinkaya F, Topaloglu H, Karabacak O, Gunlusoy B, Unal S. Efficacy of transurethral electrovaporization of the prostate with respect to standard transurethral resection. *J Endourol* 1998;**12**:591–4.

198. Netto NR, Jr, de Lima ML, Lucena R, Lavoura NS, Cortado PL, Netto MR. Is transurethral vaporization a remake of transurethral resection of the prostate? *J Endourol* 1999;**13**:591–4.

199. Nuhoğlu B, Ayyildiz A, Fidan V, Ersoy E, Huri E, Germiyanogu C. Transurethral electrovaporization of the prostate: is it any better than standard transurethral prostatectomy? 5-year follow-up. *J Endourol* 2005;**19**:79–82.

200. Shokeir AA, al Sisi H, Farage YM, el Maaboud MA, Saeed M, Mutabagani H. Transurethral prostatectomy: a prospective randomized study of conventional resection and electrovaporization in benign prostatic hyperplasia. *Br J Urol* 1997;**80**:570–4.

201. Wang ZL, Wang XF, Li B, Ji JT, Hou SC, Shao SX, *et al*. Comparative study of transurethral electrovaporization of prostate versus transurethral resection of prostate on benign prostatic hyperplasia. *Zhong Hua Nan Ke Xue* 2002;**8**:428–30.

202. Helke C, Manseck A, Hakenberg OW, Wirth MP. Is transurethral vaporesection of the prostate better than standard transurethral resection? *Eur Urol* 2001;**39**:551–7.

203. Küpeli S, Yilmaz E, Soygur T, Budak M. Randomized study of transurethral resection of the prostate and combined transurethral resection and vaporization of the prostate as a therapeutic alternative in men with benign prostatic hyperplasia. *J Endourol* 2001;**15**:317–21.

204. Abdel-Khalek M, El Hammady S, Ibrahiem E. A 4-year follow-up of a randomized prospective study comparing transurethral electrovaporization of the prostate with neodymium:YAG laser therapy for treating benign prostatic hyperplasia. *BJU Int* 2003;**91**:801–5.

205. Narayan P, Tewari A, Aboseif S, Evans C. A randomized study comparing visual laser ablation and transurethral evaporation of prostate in the management of benign prostatic hyperplasia. *J Urol* 1995;**154**:2083–8.

206. Shingleton WB, Renfroe LD, Kolski JM, Fowler JE, Jr. A randomized prospective study of transurethral electrovaporization vs laser ablation of the prostate in men with benign prostatic hypertrophy. *Scand J Urol Nephrol* 1998;**32**:266–9.

207. d'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, de la Rosette JJ. High energy thermotherapy versus transurethral resection in the treatment of benign prostatic hyperplasia: results of a prospective randomized study with 1 year of follow-up. *J Urol* 1997;**158**:120–5.

208. Dahlstrand C, Fall M, Geirsson G, Petterson DE. Transurethral microwave thermotherapy versus transurethral resection for benign prostatic hyperplasia: results of a randomized study. *J Urol* 1993;**149**:250A.

209. Dahlstrand C, Geirsson G, Walden M. Prospective randomized study between transurethral resection (TURP) and transurethral microwave treatment (TUMT) for benign prostatic hyperplasia. *Scand J Urol Nephrol Suppl* 1993;**151**:32–3.

210. Dahlstrand C, Walden M, Geirsson G, Sommar S, Pettersson S. Transurethral microwave thermotherapy versus transurethral resection for BPH. *Prog Clin Biol Res* 1994;**386**:455–61.

211. Duelund J, Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, *et al*. Prostalund feedback treatment versuis TURP: a prospective randomized multicenter study with 36 month follow-up. *Scand J Urol Nephrol* 2003;**37**(Suppl214):34–5.

212. Floratos DL, Kiemeney LA, Rossi C, Kortmann BB, Debruyne FM, de la Rosette JJ. Long-term follow-up of randomized transurethral microwave thermotherapy versus transurethral prostatic resection study. *J Urol* 2001;**165**:1533–8.

213. Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de la Rosette JJ. A randomized study comparing high-energy TUMT to TURP: quality-of-life results. *Eur Urol* 2000;**38**:569–75.

214. Kobelt G, Spangberg A, Mattiasson A. The cost of feedback microwave thermotherapy compared with transurethral resection of the prostate for treating benign prostatic hyperplasia. *BJU Int* 2004;**93**:543–8.

215. Nordling J, Wagrell L, Larson T, Duelund J, Kroyer K, Mattiasson A. ProstaLund feedback treatment (PLFT) vs TURP: a prospective randomized muliticenter study with 36 month follow up. *BJU Int* 2005;**95**(Suppl 5):75.

216. Wagrell L, Schelin S, Nordling J, Larsson T, Mattiasson A. Prostalund microwave feedback treatment compared with TURP for treatment of BPH: a prospective randomized multicentre study. *Aust NZ J Surg* 2003;**73**:A146.

217. Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, Schain M, *et al*. ProstaLund microwave feedback treatment compared with TURP for treatment of BHP: a prospective randomized multicenter study with 24 months folllow up. *J Urol* 2003;**169**(Suppl 4):1748.

218. Walden M, Acosta S, Carlsson P, Pettersson S, Dahlstrand C. A cost-effectiveness analysis of transurethral resection of the prostate and transurethral microwave thermotherapy for treatment of benign prostatic hyperplasia: two-year follow-up. *Scand J Urol Nephrol* 1998;**32**:204–10.

219. Albala DM, Koleski F, Nuzzarello J, Davis BE, Eure GR, Andriole G, *et al*. Periurethral prostatic microwave thermotherapy using the Thermatrx TMX-2000TM: follow-up of a randomized, blinded, sham-controlled study in patients with BPH. *J Urol* 2000;**163**:269.

220. Albala DM, Andriole G, Davies B. Transurethral microwave thermotherapy (TUMT) using the Thermatrx TMX-2000: durability exhibited in a study comparing TUMT with a sham procedure in patients with benign prostatic hyperplasia. Abstract no. 1746. 2003. Annual Meeting of the American Urological Association.

221. Albala DM, Andriole G, Davies B, Eure GR, Kabalin JN, Lingeman JE, *et al*. Transurethral microwave thermotherapy (TUMT) using the Thermatrx TMX-2000: long-term results in a study comparing TUMT with a sham procedure in patients with benign prostatic hyperplasia. Abstract no. 1551. 2005. Annual Meeting of the American Urological Association.

222. Bdesha AS, Bunce CJ, Kelleher JP, Snell ME, Vukusic J, Witherow OR. Transurethral microwave treatment for benign prostatic hypertrophy: a randomised controlled clinical trial. *BMJ* 1993;**306**:1293–6.

223. de la Rosette JJ, de Wildt MJ, Alivizatos G, Froeling FM, Debruyne FM. Transurethral microwave thermotherapy (TUMT) in benign prostatic hyperplasia: placebo versus TUMT. *Urology* 1994;**22**:58–63.

224. Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de la Rosette JJ. Quality of life assessment in patients treated with lower energy thermotherapy (Prostasoft 2.0): results of a randomized transurethral microwave thermotherapy versus sham study. *J Urol* 1997;**158**:1839–44.

225. Kabalin JN, Albala DM, Koleski F, Andriole G, Sundaram C, Davis BE, *et al*. Office-based transurethral microwave thermotherapy for benign prostatic hyperplasia (BPH) using the TherMatrxTM TMx-2000TM: results of a multi-center prospective randomized sham-controlled trial. *J Urol* 2001;**165**:367–8.

226. Roehrborn C, Sech S, Preminger G, Cohen T, Perlmutter A, Razvi H, *et al*. A randomized, blinded study comparing microwave thermotherapy (Dornier Urowave) with a sham procedure in patients with clinical benign prostatic hyperplasia (BPH). *J Endourol* 1997;**11**(Suppl1):S155.

227. Roehrborn CG, Preminger G, Newhall P, Denstedt J, Razvi H, Chin LJ, *et al*. Microwave thermotherapy for benign prostatic hyperplasia with the Dornier Urowave: results of a randomized, double-blind, multicenter, sham-controlled trial. *Urology* 1998;**51**:19–28.

228. Tan AH, Nott L, Hardie WR, Chin JL, Denstedt JD, Razvi H. Long-term results of microwave thermotherapy for symptomatic benign prostatic hyperplasia. *J Endourol* 2005;**19**:1191–5.

229. Bruskewitz R, Issa MM, Roehrborn CG, Naslund MJ, Perez-Marrero R, Shumaker BP, *et al*. A prospective, randomized 1-year clinical trial comparing transurethral needle ablation to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia. *J Urol* 1998;**159**:1588–93.

230. Mostafid AH, Harrison NW, Thomas PJ, Fletcher MS. A prospective randomized trial of interstitial radiofrequency therapy versus transurethral resection for the treatment of benign prostatic hyperplasia. *Br J Urol* 1997;**80**:116–22.

231. Naslund M, Oesterling JE, Issa M, Roehrborn CG, Bruskewitz R, Perez-Marrero R, *et al*. Long term follow-up of a prospective, randomized clinical trial comparing transurethral needle ablation (TUNA) to transurethral resection of the prostate (TURP) for the treatment of benign prostatic hyperplasia (BPH). *J Endourol* 1997;**11**:S188.

232. Naslund M, Perez-Marrero R, Roehrborn C, Bruskewitz R, Issa M. Intermediate term outcomes of TUNA for BPH: 36 month results of the TUNA vs TURP US randomized study. *J Urol* 1999;**161**:389.

233. Roehrborn CG, Burkhard FC, Bruskewitz RC, Issa MM, Perez-Marrero R, Naslund MJ, *et al*. The effects of transurethral needle ablation and resection of the prostate on pressure flow urodynamic parameters: analysis of the United States randomized study. *J Urol* 1999;**162**:92–7.

234. Anson K, Nawrocki J, Buckley J, Fowler C, Kirby R, Lawrence W, *et al*. A multicenter, randomized, prospective study of endoscopic laser ablation versus transurethral resection of the prostate. *Urology* 1995;**46**:305–10.

235. Brookes ST, Donovan JL, Peters TJ, Abrams P, Neal DE. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomised controlled trial. *BMJ* 2002;**324**:1059–61.

236. Donovan JL, Brookes ST, Kennedy LG, Abrams P, Peters TJ, Neal DE. The CLasP randomised controlled trial: comparing laser therapy, conservative management and TURP for men with lower urinary tract symptoms. *J Urol* 1998;**159**:248.

237. Kabalin JN. Laser prostatectomy performed with a right angle firing neodymium:YAG laser fiber at 40 watts power setting. *J Urol* 1993;**150**:95–9.

238. Aagaard J, Chopin D, Knes J, Madsen PO. Transurethral resection TURP vs incision TUIP of the prostate: a prospective randomized study. *J Urol* 1990;**143**:411A.

239. Riehmann M, Knes J, Madaan S, Bruskewitz R. Transurethral resection (TURP) versus incision (TUIP) of the prostate: a prospective randomized study. *J Urol* 1993;**149**(Suppl 4):323A.

240. Sparwasser C, Riehmann M, Knes J, Madsen PO. Long-term results of transurethral prostate incision (TUIP) and transurethral prostate resection (TURP). A prospective randomized study. *Urologe (Ausg A)* 1995;**34**:153–7.

241. Briganti A, Naspro R, Vavassori I, Suardi N, Salonia A, Mazzoccoli B, *et al*. Impact of holmium laser enucleation (HoLEP) versus transurethral resection (TURP) of the prostate on sexual function: results of a prospective multicentric randomized trial. *J Urol* 2004;**171**:398.

242. Briganti A, Naspro R, Vavassori I, Suardi N, Salonia A, Mazzoccoli B, *et al*. Impact of holmium laser enucleation (HoLEP) versus transurethral resection (TURP) of the prostate on sexual function: results of a prospective multicentric randomized trial. *Eur Urol Suppl* 2004;**3**:144.

243. Fraundorfer MR, Gilling PJ, Kennett KM, Dunton NG. Holmium laser resection of the prostate is more cost-effective than transurethral resection of the prostate: results of a randomized prospective study. *Urology* 2001;**57**:454–8.

244. Gilling P, Westenberg A, Kennett KM, Fraundorfer MR. Holmium laser resection of the prostate (HOLRP) vs transurethral resection of the prostate (TURP): results at 4 years. *Aust NZ J Surg* 2003;**73**:A145.

245. Gilling PJ, Fraundorfer MR, Westenberg AM, Neill MG, Frampton CM, Kennett KM. Relief of bladder outflow obstruction (BOO) following HoLEP and TURP: a pooled analysis of data from 4 randomized trials. *BJU Int* 2005;**95**(Suppl5):74.

246. Kuntz RM, Ahyai S, Lehrich K. Holmium laser enucleation vs TURP: a randomized prospective study with 2 years of follow-up. *BJU Int* 2003;**91**(Suppl2):71.

247. Montosori F, Naspro R, Salonia A, Suardi N, Briganti A, Zanoni M. Holmium laser enucleation versus transurethral resection of the prostate: results from a two-centre prospective randomized trial in patients with obstructive benign prostatic hyperplasia. *J Urol* 2004;**171**:409.

248. Tan AH, Gilling PJ, Kennett KM, Frampton C, Westenberg AM, Fraundorfer MR. A randomized trial comparing holmium laser enucleation of the prostate with transurethral resection of the prostate for the treatment of bladder outlet obstruction secondary to benign prostatic hyperplasia in large glands (40 to 200 grams). *J Urol* 2003;**170**:1270–4.

249. Carter A, Sells H, Speakman M, Ewings P, O'Boyle P, MacDonagh R. Quality of life changes following KTP/Nd:YAG laser treatment of the prostate and TURP. *Eur Urol* 1999;**36**:92–8.

250. Jenkinson C, Gray A, Doll H, Lawrence K, Keoghane S, Layte R. Evaluation of index and profile measures of health status in a randomized controlled trial. Comparison of the Medical Outcomes Study 36-Item Short Form Health Survey, EuroQol, and disease specific measures. *Med Care* 1997;**35**:1109–18.

251. Keoghane S, Cranston D, Lawrence K, Doll H. The Oxford laser prostate trial: a prospective randomised controlled trial of contact vaporisation of the prostate versus TURP. *J Urol* 1995;**153**:230A.

252. Keoghane SR, Doll HA, Lawrence KC, Jenkinson CP, Cranston DW. The Oxford Laser Prostate Trial: sexual function data from a randomized controlled clinical trial of contact laser prostatectomy. *Eur Urol* 1996;**30**:424–8.

253. Keoghane SR, Lawrence KC, Jenkinson CP, Doll HA, Chappel DB, Cranston DW. The Oxford Laser Prostate Trial: sensitivity to change of three measures of outcome. *Urology* 1996;**47**:43–7.

254. Keoghane SR, Cranston DW, Lawrence KC, Doll HA, Fellows GJ, Smith JC. The Oxford Laser Prostate Trial: a double-blind randomized controlled trial of contact vaporization of the prostate against transurethral resection; preliminary results. *Br J Urol* 1996;**77**:382–5.

255. Keoghane SR, Sullivan ME, Doll HA, Kourambas J, Cranston DW. Five-year data from the Oxford Laser Prostatectomy Trial. *BJU Int* 2000;**86**:227–8.

256. Mottet N, Anidjar M, Costa P, Louis JF, Teillac P, Duc A. A randomized study comparing the holmium-YAG vaporisation and the transurethral resection of symptomatic BPH. *J Endourol* 1997;**11**(Suppl1):S160.

257. Pearcy R, Carter A, Sells H, O'Boyle P, MacDonagh R, Speakman M, *et al*. Long term follow up of hybrid KITP/ND:YAG laser treatment of the prostate versus TURP: a prospective randomised trial, 18 month results. *J Urol* 1999;**161**:390.

258. Shingleton WB, Terrell F, Renfroe DL, Kolski JM, Fowler JE, Jr. A randomized prospective study of laser ablation of the prostate versus transurethral resection of the prostate in men with benign prostatic hyperplasia. *Urology* 1999;**54**:1017–21.

259. Shingleton WB, Farabaugh P. Prospective randomized study of laser prostatectomy and transurethral resection of the prostate in men with benign prostatic hyperplasia: 3 year follow-up. *J Urol* 2001;**165**(Suppl 5):297.

260. Tuhkanen K, Heino A, Ala-Opas M. Hybrid laser treatment compared with transurethral resection of the prostate for symptomatic bladder outlet obstruction caused by a large benign prostate: a prospective, randomized trial with a 6-month follow-up. *BJU Int* 1999;**84**:805–9.

261. Tuhkanen K, Heino A, Ala-Opas M. Contact laser prostatectomy compared to TURP in prostatic hyperplasia smaller than 40 ml. Six-month follow-up with complex urodynamic assessment. *Scand J Urol Nephrol* 1999;**33**:31–4.

262. van Melick HH, van Venrooij GE, Eckhardt MD, Boon TA. A randomized controlled trial comparing transurethral resection of the prostate, contact laser prostatectomy and electrovaporization in men with benign prostatic hyperplasia: urodynamic effects. *J Urol* 2002;**168**:1058–62.

263. van Melick HH, van Venrooij GE, Eckhardt MD, Boon TA. A randomized controlled trial comparing transurethral resection of the prostate, contact laser prostatectomy and electrovaporization in men with benign prostatic hyperplasia: analysis of subjective changes, morbidity and mortality. *J Urol* 2003;1**69**:1411–16.

264. Hammadeh MY, Madaan S, Singh M, Philp T. Two-year follow-up of a prospective randomised trial of electrovaporization versus resection of prostate. *Eur Urol* 1998;**34**:188–92.

265. Hammadeh MY, Madaan S, Singh M, Philp T. Two years follow up of a prospective randomised trial of electro-vaporisation of the prostate vs standard TURP. *J Endourol* 1998;**12**:S175.

266. Hammadeh MY, Fowlis GA, Singh M, Philp T. Transurethral electrovaporization of the prostate – a possible alternative to transurethral resection: a one-year follow-up of a prospective randomized trial. *Br J Urol* 1998;**81**:721–5.

267. Hammadeh MY, Madaan S, Singh M, Philp T. Three years follow up of a prospective randomised trial comparing transurethral electrovaporization of the prostate to standard TURP. *J Endourol* 1999;**13**:A29.

268. Hammadeh MY, Madaan S, Singh M, Philp T. A 3-year follow-up of a prospective randomized trial comparing transurethral electrovaporization of the prostate with standard transurethral prostatectomy. *BJU Int* 2000;**86**:648–51.

269. Hammadeh MY, Madaan S, Hines J, Philp T. The efficacy and durability of transurethral electrovaporisation of the prostate: 5 year result of a prospective randomised trial. *Eur Urol Suppl* 2003;**2**:168.

270. McAllister WJ, Karim O, Plail RO, Samra DR, Steggall MJ, Yang Q, *et al*. Transurethral electrovaporization of the prostate: is it any better than conventional transurethral resection of the prostate? *BJU Int* 2003;**91**:211–14.

271. Puppo P, Perachino M, Breda G, Boccafoschi C, Comeri G, Francesca F, *et al*. Transurethral electrovaporization of the prostate (T.V.P.): a

multicentric randomized comparative study vs TURP. *J Urol* 1996;**155**(Suppl 5):408A

272. Love CJ, Dowling C, Pham T, Tan A, McFarlane JP, Dunsmuir WD. Gyrus (R) bipolar electrovaporization versus transurethral resection of the prostate: a randomized prospective trial with 1-year follow-up. *J Urol* 2003;**169**:390.

273. Kok ET, McDonnell J, Stolk EA, Stoevelaar HJ, Busschbach JJV. The valuation of the international prostate symptom score (IPSS) for use in economic evaluations. *Eur Urol* 2002;**42**:491–7.

274. Tweedie RL, Scott DJ, Biggerstaff BJ, Mengersen KL. Bayesian meta-analysis, with application to studies of ETS and lung cancer. *Lung Cancer* 1996;**14**:S171–94.

275. Newcombe RG. Towards a reduction in publication bias. *BMJ* 1987;**295**:656–9.

276. Thornton A, Lee P. Publication bias in meta-analysis: its causes and consequences. *J Clin Epidemiol* 2000;**53**:207–16.

277. Greenland S. Quality scores are useless and potentially misleading. [Reply to "Re: A critical look at some popular analytical methods".] *Am J Epidemiol* 1994;**140**:300–1.

278. Greenland S, O'Rourke K. On the bias produced by quality scores in meta-analysis, and a hierarchial view of proposed solutions. *Biostatistics* 2001;**2**:463–71.

279. Juni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ* 2001;**323**:42–6.

280. Soares HP, Daniels S, Kumar A, Clarke M, Scott C, Swann S, *et al*. Bad reporting does not mean bad methods for randomised trials: observational study of randomised controlled trials performed by the Radiation Therapy Oncology Group. *BMJ* 2004;**328**:22–4.

281. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**:408–12.

282. Schulz KF. Assessing allocation concealment and blinding in randomised controlled trials: why bother? *Evid Based Nurs* 2001;**4**:4–6.

283. Wiebe N, Vandermeer B, Platt RW, Klassen TP, Moher D, Barrowman NJ. A systematic review identifies a lack of standardization in methods for handling missing variance data. *J Clin Epidemiol* 2006;**59**:342–53.

284. Barry MJ, Fowler FJ, Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen–Iversen, Boyarsky and Maine Medical Assessment Program symptom indexes. Measurement Committee of the American Urological Association. *J Urol* 1992;**148**:1558–63.

285. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al*. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;**8**:1–158.

286. National Institute for Clinical Excellence. *Guide on the methods of technology appraisal (reference N0515).* National Institute for Clinical Excellence, 2004. URL: www.nice.org.uk/page.aspx?o=201973. Accessed September 2006.

287. Djavan B, Roehrborn CG, Shariat S, Ghawidel K, Marberger M. Prospective randomized comparison of high energy transurethral microwave thermotherapy versus alpha-blocker treatment of patients with benign prostatic hyperplasia. *J Urol* 1999;**161**:139–43.

288. Djavan B, Seitz C, Roehrborn CG, Remzi M, Fakhari M, Waldert M, *et al*. Targeted transurethral microwave thermotherapy versus alpha-blockade in benign prostatic hyperplasia: outcomes at 18 months. *Urology* 2001;**57**:66–70.

289. Bouchier-Hayes DM, Anderson P, Van Appledom S, Bugeja P, Costello AJ. A randomised trial comparing photoselective vaporization of the prostate (PVP) and transurethral resection of the prostate (TURP) in treatment of LUTS. *J Urol* 2006;**175**:463.

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