Systematic review and economic modelling of effectiveness and cost utility of surgical treatments for men with benign prostatic enlargement

T Lourenco,¹ N Armstrong,² J N’Dow,³* G Nabi,³ M Deverill,² R Pickard,⁴ L Vale,¹ G MacLennan,¹ C Fraser,¹ S McClinton,³ S Wong,¹ A Coutts,¹ G Mowatt¹ and A Grant¹

¹Health Services Research Unit, Institute of Applied Health Sciences, University of Aberdeen, UK
²Health Economics Research Unit, Centre of Health Services Research, University of Newcastle, UK
³Academic Urology Unit, Department of Surgery, University of Aberdeen, UK
⁴Department of Urology, School of Surgical and Reproductive Sciences, University of Newcastle, UK

*Corresponding author

Executive summary

Health Technology Assessment 2008; Vol. 12: No. 35
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 vapourisation, transurethral vapourisation 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 vapourisation (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.

**Publication**

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. ‘Health technologies’ are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’.

The HTA Programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Second, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

### Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed ‘systematic’ when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

Editor-in-Chief: Professor Tom Walley

Series Editors: Dr Aileen Clarke, Dr Peter Davidson, Dr Chris Hyde, Dr John Powell, Dr Rob Riemsma and Professor Ken Stein