An evaluation of the economic costs and patient-related consequences of treatments for benign prostatic hyperplasia

Disantostefano R L, Biddle A K, Lavelle J P

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined various treatments for benign prostatic hyperplasia (BPH). These included watchful waiting (WW), pharmaceuticals (alpha-blockers, 5-alpha-reductase inhibitors (5-ARIs), combined therapy), transurethral microwave thermotherapy (TUMT) and transurethral resection of the prostate (TURP).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The patient population comprised men with uncomplicated BPH, displaying moderate-to-severe lower urinary tract symptoms (classified using the IPSS). The authors considered five hypothetical age cohorts (45, 55, 65, 75 and 85 years old) for the correlation of age with costs and consequences.

Setting
The setting was primary care and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was drawn from data published between 1994 and December 2005. The unit costs were drawn from evidence published between 2003 and 2005 in order to derive annual costs for the USA in 2004.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.

Modelling
A decision analysis, using a Markov model and a 1-year time cycle, was used to examine the cost and clinical consequences of different treatments for BPH over 20 years. The model used the same structure as a reported cost-utility model (DiSantostefano et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details) but disease progression was defined in two ways. In one way it was defined by the probability of surgery (as in the cost-utility model), while in the other, a composite definition involving clinical and patient-reported measures was used. The model was evaluated under different scenarios of treatment switching, and the authors assumed that treatment failures requiring surgery resulted in TURP. Transition probabilities for WW were estimated primarily from placebo estimates reported in clinical trials.
Outcomes assessed in the review
Input parameters included:

- the annual probabilities of improvement with and without various adverse events,
- failure requiring first or second TURP,
- treatment failure requiring surgery,
- days of hospital stay following TURP,
- days of catheterisation after an operation (TUMT and TURP),
- treatment switching,
- pharmaceutical compliance,
- urethral stricture or bladder neck contracture,
- all-cause mortality, and
- BPH disease progression (a composite outcome of clinical measures and patient-reported outcomes).

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
The authors stated that the annual probabilities for the Markov model were estimated from a thorough literature search (1991 to 2004), but no detail of the sources was provided.

Criteria used to ensure the validity of primary studies
It was stated that all estimates were derived from published reports, including systematic reviews when possible. No further detail was provided.

Methods used to judge relevance and validity, and for extracting data
The authors stated that the main source of data was the American Urological Association's (AUA) guidelines, which included the period from 1991 to early 2000, with additional information from 2000 to 2005 gathered to supplement information on newer treatments. A justification for the approach taken was not provided.

Number of primary studies included
Approximately 12 primary studies were included in the review as sources of effectiveness evidence.

Methods of combining primary studies
The primary studies were not formally combined, although the authors made assumptions about the rates of switching based on their review of clinical trials and database studies.

Investigation of differences between primary studies
The authors did not formally investigate differences between the primary studies. However, they did describe an adjustment made to make the rate of disease progression in one trial more comparable to the rate of treatment failure in...
another trial (removal of death from the latter trial’s definition of treatment failure).

Results of the review
The main treatment effectiveness parameters used in the model were the probabilities of disease progression and surgery.

The mean probability of disease progression (with beta distribution parameters in brackets) was 0.044 (30.7 to 677.3) for WW, 0.027 (19.7 to 708.3) for alpha-blockers, 0.029 (21 to 703) for 5-ARIs, 0.015 (11.3 to 742.7) for combined therapy, and 0.012 (3.5 to 276.6) for TURP.

The mean probability of surgery (with beta distribution parameters in brackets) was 0.013 (9 to 689) for WW, 0.013 (9.4 to 718.6) for alpha-blockers, 0.005 (2.6 to 720.4) for 5-ARIs, 0.004 (3 to 750) for combined therapy, 0.071 (0.036 to 0.110) for TUMT, and 0.021 (0.011 to 0.032) for TURP.

Further details of inputs were tabulated (e.g. proportions switching to each therapy, probability of improvement with various adverse events).

Measure of benefits used in the economic analysis
No summary measure of benefits was used. In effect, a cost-consequences analysis was performed.

Direct costs
The costs and outcomes were discounted at a rate of 3% per annum. The costs and the quantities were analysed separately. It was unclear how resource use was identified, but it would appear to have been derived from both published studies and author assumptions (see DiSantostefano et al. 2006). The unit costs were drawn from a managed-care claims database, Medicare fee schedules and average wholesale prices of pharmaceuticals. Only direct health care costs were included. Prices for 2004 were used.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs (i.e. productivity costs) were not included, despite the authors stating that a societal perspective had been adopted.

Currency
US dollars ($).

Sensitivity analysis
Variability was measured probabilistically, using 1,000 Monte Carlo simulations. The mean and 5th and 95th percentiles were calculated for the costs and treatment effectiveness estimates of interest. Ranges were derived from both the literature and authors’ assumptions. To examine inter-relationships among treatments, the correlation between the probability of no improvement between combined therapy and monotherapy was varied from zero to one. Most costs were varied deterministically (+/- 50%), although the costs of TUMT and TURP were varied assuming a normal distribution.

Estimated benefits used in the economic analysis
In the base-case cohort of 65-year-olds, the cumulative proportion of men with BPH progression was lowest for TURP
(15.6%) and highest for WW (43.5%) over 20 years (188% for combined therapy, 30.6% for alpha-blockers, 32.4% for 5-ARIs).

The cumulative probability of TURP was lowest for combined therapy (7.8%), followed by 5-ARIs (8.5%), alpha-blockers (15.4%) and WW (15.6%).

A cohort of 1,000 men initially treated with TUMT or TURP were expected to spend 1,579 and 3,302 days in hospital, respectively. Similarly, 1,000 men initially treated with WW or an alpha-blocker were expected to spend 511 or 504 days in hospital, while those treated with 5-ARIs or combined therapy were expected to spend 281 or 256 days in hospital.

The expected number of catheterisation days was highest for TUMT (15,775 days), followed by TURP (4,501 days).

Other model outcomes for the alternative age cohorts were presented in the paper.

**Cost results**

For the base-case (1,000 men aged 65 years who could switch among pharmaceuticals or WW and require TURP), the costs of treatment over 20 years ranged from $4.4 million for WW to $11.6 million for combined therapy ($6.7 million for alpha-blockers, $7.9 million for TUMT, $8.4 million for TURP, $8.8 million for 5-ARIs).

Although the 20-year total costs decreased for each successive age cohort, the ordering remained the same.

**Synthesis of costs and benefits**

The costs and benefits were not combined.

**Authors’ conclusions**

The authors noted that, depending on the value placed on costs and outcomes, the best treatment for benign prostatic hyperplasia (BPH) varies. Alpha-blockers are the least expensive treatment, but they have less effect on clinical outcomes and have the highest rate of BPH progression. Combined therapy is expensive in the long-run. Transurethral resection of the prostate (TURP) remains the "gold standard" and is the most effective treatment but the most invasive. The authors noted that their previous cost-utility model showed that the most cost-effective alternative depends on the severity of baseline symptoms.

**CRD COMMENTARY - Selection of comparators**

The comparators appeared to comprise all available treatment alternatives for BPH in the USA. This was not explicitly stated but implied via criticism of previous models for their scope of treatments examined. Both surgical and non-surgical treatments were included. You should decide if the comparators represent all the alternatives relevant to your own setting.

**Validity of estimate of measure of effectiveness**

The authors stated a thorough, though not systematic, review of the literature had been undertaken. The searches and judgements used in the review were not described, so it was unclear whether the review was conducted systematically to identify all relevant research and minimise bias. The authors generally used data from the available studies selectively, and do not appear to have combined the effectiveness estimates. In the absence of detailed data on switching between non-surgical treatments, the authors made simplifying assumptions after reviewing two major clinical trials. The authors clearly reported the sources of the effectiveness estimates and the statistical distributions assigned to the parameters. A sensitivity analysis was conducted using probabilistic distributions, which was appropriate for the types of parameter inputs within the model. The use of a probabilistic sensitivity analysis helps address parameter uncertainty.
Validity of estimate of measure of benefit
The estimation of benefits was modelled using 1,000 Monte Carlo simulations of a Markov model. This method was appropriate. The authors did not derive a single measure of benefit, thus the analysis was classed as a cost-consequences study. The authors noted a published cost-utility analysis founded on the same health economic model (DiSantostefano et al. 2006).

Validity of estimate of costs
Although the authors reported that the costs were estimated from a societal perspective, productivity costs were not included. It was unclear whether adverse events incurred relevant costs of treatment within the model; their omission might have affected the accuracy of the conclusions. Other categories of costs were appropriately included, with quantities being derived using authors’ assumptions and published studies. Variability was included for hospital stay and catheterisation stay only. The unit costs were taken from a national research database, a managed-care claims database and Medicare fee schedules. A sensitivity analysis investigating +/- 50% on all costs was performed, while normal distributions were applied to the costs of TUMT and TURP. Cost assumptions were not described in full as the reader was referred to the cost-utility analysis published separately. It is likely that sufficient information was reported to allow the reader to decide whether the costs reflect the level of costs incurred in their own setting for the various treatment alternatives. Discounting at a rate of 3% per annum was applied. The author used costs prevailing in the USA in 2004.

Other issues
The authors made appropriate comparisons of their approach with those from other studies in the introductory section. However, they did not discuss the comparability of their findings. In addition, the issue of generalisability to other settings was not addressed. The authors presented results for only three of the five age-banded cohorts, but stated that the ordering of treatment alternatives remained the same for each outcome measure and each age cohort and described how the absolute value of the outcome increased or decreased with age. Therefore, it would appear that the results were presented selectively but without bias. The study modelled men with moderate-to-severe BPH and this was reflected in the authors’ conclusions.

The authors reported a number of limitations to their study. First, they did not examine cost-consequences according to the level of prostate-specific antigen, symptom levels and other sub-groups, owing to a lack of data. Second, differences in study inclusion criteria and study duration might have resulted in some inappropriate comparisons across treatments. Third, a lack of long-term studies and differences between surgical and non-surgical trial populations might have biased the results in favour of pharmaceuticals. Finally, the costs of the included pharmaceuticals are expected to decrease as patents expire and new agents come on the market. A cost-utility analysis derived from this work was published separately (DiSantostefano et al. 2006).

Implications of the study
The authors stated that more research is needed to determine the long-term durability of TUMT. Data are also needed to inform the modelling of switching among treatments over time. The importance of direct elicitation of patient preferences was emphasised.

Source of funding
Supported by the Agency for Healthcare Research and Quality.

Bibliographic details

PubMedID
16542339
DOI
10.1111/j.1464-410X.2005.06089.x

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
5-alpha Reductase Inhibitors; Adrenergic alpha-Antagonists /economics /therapeutic use; Aged; Aged, 80 and over; Combined Modality Therapy /economics; Cost-Benefit Analysis; Disease Progression; Hospitalization /economics /statistics & numerical data; Humans; Hyperthermia, Induced /economics; Male; Markov Chains; Middle Aged; Prostatic Hyperplasia /economics /therapy; Transurethral Resection of Prostate /economics; Treatment Outcome

AccessionNumber
22006000801

Date bibliographic record published
30/11/2006

Date abstract record published
30/11/2006