Cost-effectiveness of combination therapy for treatment of benign prostatic hyperplasia: a model based on the findings of the Combination of Avodart and Tamsulosin trial

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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.

CRD summary
The study examined the cost-effectiveness of fixed-dose combination therapy (tamsulosin plus dutasteride) for benign prostatic hyperplasia (benign enlargement of the prostate gland) versus tamsulosin monotherapy, dutasteride monotherapy or watchful waiting. The authors concluded that combination therapy was cost-effective at a willingness-to-pay threshold at or above EUR 6,000. The analysis used a conventional cost-effectiveness framework, but some aspects were not reported in detail. The authors' conclusions appear valid but an incremental analysis among strategies compared would have been useful.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of combination therapy with tamsulosin and dutasteride for benign prostatic hyperplasia compared with alpha-blocker monotherapy, 5-alpha reductase inhibitor monotherapy or watchful waiting using data from a clinical trial.

Interventions
The four treatments examined were watchful waiting, alpha-blocker monotherapy (tamsulosin), 5-alpha reductase inhibitor monotherapy (dutasteride), and fixed-dose combination therapy of tamsulosin plus dutasteride.

Location/setting
Norway/secondary care.

Methods
Analytical approach:
The analysis was based on a previously published decision model that was constructed as a semi-Markov process with four-year and lifetime horizons. The model was expanded to include all relevant strategies. The authors stated that a limited societal perspective was adopted (payer perspective in the base case).

Effectiveness data:
Clinical inputs were taken from selectively identified sources. Most data on patients' characteristics and treatment effect for combined and monotherapy options came from the Combination of Avodart and Tamsulosin (CombAT) trial (Roehrborn, et al. 2008, see 'Other Publications of Related Interest' below for bibliographic details). Additional data for watchful waiting came from the Medical Therapy of Prostatic Symptoms (MTOPS) trial (McConnell, et al. 2003 see 'Other Publications of Related Interest' below for bibliographic details). Mortality rates were taken from Norwegian life tables. Rates of acute urinary retention/transurethral resection of the prostate (AUR/TURP) were the primary inputs of the model.

Monetary benefit and utility valuations:
Utility valuations were taken from other cost-effectiveness studies on benign prostatic hyperplasia which were not described.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure. They were discounted at an annual rate of 3.5%.

Cost data:
The costs included drugs, physician visits, and routine prostate-specific antigen blood tests. Recommended dosing regimens were used to reflect pattern of drug consumption. Generic drug prices were used for tamsulosin and finasteride, while a branded price was used for dutasteride. Sources of costs were not explicitly stated; they appear to have been based on a previous model. Costs were in Euros (EUR). Costs accrued after the first year were discounted at a rate of 3.5%.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were carried out. The various alternative scenarios considered were: inclusion of indirect costs associated with work or leisure time lost because of the disease; an alternative combination therapy with finasteride and tamsulosin; variations in utility valuations; restriction to patients with severe symptoms, and different relative rates of events.

Results
In the four-year model, watchful waiting expected total costs were EUR 676 and 3.20 QALYs per patient. Dutasteride monotherapy expected total costs were EUR 1,601 and 3.30 QALYS per patients. Tamsulosin monotherapy expected total costs were EUR 1,053 and 3.29 QALYs per patient. Fixed-dose combination therapy expected total costs were EUR 1,555 and 3.34 QALYS per patient. In comparison with watchful waiting, the incremental cost per QALY gained was EUR 9,294 with dutasteride, EUR 4,265 with tamsulosin, and EUR 6,092 with combination therapy.

In the lifetime model, watchful waiting expected total costs were EUR 1,970 and 9.69 QALYs per patients. Dutasteride expected total costs were EUR 4,840 and 10.09 QALYS per patient. Tamsulosin expected total costs were EUR 3,093 and 9.96 QALYS per patient. Combination therapy expected total costs were EUR 4,738 and 10.24 QALYS per patient. In comparison with watchful waiting, the incremental cost per QALY gained was EUR 7,274 with dutasteride, EUR 4,184 with tamsulosin, and EUR 5,065 with fixed-dose combination therapy.

Key model drivers were the intensity of follow-up in the watchful waiting arm and the probability of transurethral resection of the prostate. Overall, the ranking of the strategies did not change substantially.

The probabilistic analysis showed that fixed-dose combination therapy was the preferred strategy at a willingness to pay of EUR 6,000 or more. For lower figures, alpha-blocker monotherapy (tamsulosin) was preferred, although there was considerable uncertainty around this threshold.

Authors’ conclusions
The authors concluded that fixed-dose combination therapy for benign prostatic hyperplasia was a cost-effective strategy at a willingness-to-pay threshold at or above EUR 6,000.

CRD commentary
Interventions:
The selection of the comparators was appropriate as all commonly used treatments for patients with benign prostatic hyperplasia were used. No switch among treatments was assumed.

Effectiveness/benefits:
The treatment effect for combination therapy and monotherapy options was taken from a head-to-head clinical trial with relatively long follow-up. This appeared to be a valid source of data, although few details on the study were provided in the paper. Similarly, data for watchful waiting were taken from a clinical trial.

The dimension of quality of life is particularly relevant for this patient population, so the use of QALYs appears to have been appropriate to capture the health benefits of these treatments. Limited information on the sources used to derive utility valuations was provided.

Costs:
Costs were limited to the payer perspective in the base case, while some costs associated to productivity losses were included in the scenario analysis. In general, little information on resource use and unit costs was provided, as cost data were taken from a previously published cost-effectiveness analysis. It was likely that costs reflected the Norwegian setting. Some costs were varied in the sensitivity analysis. The discount rate was reported, but the price year was not given, which would limit reflation exercises.

Analysis and results:
Incremental cost-effectiveness ratios were only calculated for watchful waiting, while no direct comparisons among monotherapy options and combination therapy were made. This represented a limitation of the analysis. It appeared that had the incremental cost per QALY of combination therapy versus monotherapy options been calculated, this would have shown a good value for money. Uncertainty was investigated using deterministic and probabilistic sensitivity analyses; the results were clearly illustrated. However, the probabilistic sensitivity analysis was likely to have been based on a first-order rather than a second-order approach. Conventional discounting was applied to both costs and benefits. Key details of the decision model and transition patterns were appropriately reported. The study results were clearly reported for all treatments and for the two time horizons of the model. Study results were likely to be valid in other settings with similar relative drug prices.

Concluding remarks:
The analysis used a conventional cost-effectiveness framework, but some aspects of the modelling study were not extensively reported. The authors’ conclusions appear valid but an incremental analysis among strategies compared would have been useful.

Funding
The study was sponsored by GlaxoSmithKline (manufacturers of dutasteride and tamsulosin). One author was an employee of GlaxoSmithKline at the time of writing.

Bibliographic details

PubMedID
21933326

DOI
10.1111/j.1464-410X.2011.10511.x

Original Paper URL

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
5-alpha Reductase Inhibitors /administration & dosage /economics; Adrenergic alpha-1 Receptor Antagonists /administration & dosage /economics; Aged; Azasteroids /administration & dosage /economics; Cost-Benefit Analysis; Drug Therapy, Combination; Dutasteride; Humans; Male; Markov Chains; Middle Aged; Prostatic Hyperplasia /drug therapy /economics; Sulfonamides /administration & dosage /economics

AccessionNumber
22012010633

Date bibliographic record published
08/06/2012

Date abstract record published
14/11/2012