Management of ocular hypertension: a cost-effectiveness approach from the ocular hypertension treatment study

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 assessed medical treatment (any hypotensive medication) for patients with ocular hypertension. Ocular hypertension was defined as an intraocular pressure (IOP) of at least 24 mmHg.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The target patient population included all patients with an IOP of at least 24 mmHg who had not yet begun to develop POAG.

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

Dates to which data relate
The effectiveness evidence was drawn from studies published between 1998 and 2006, as well as some previously unpublished data from the OHTS (Kass et al. 2002) and a prevalence study. The resource use data were drawn from the OHTS (medications) and published literature (management of progressive disease) between 2003 and 2006. The price year was 2005.

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The effectiveness data were derived from a review or synthesis of published studies and some unpublished data.

Modelling
A Markov model was constructed to assess the costs and consequences of treatment of the entire disease process over a patient’s lifetime. The health states used in the model were ocular hypertension not treated and treated, POAG Stage 1 to 5, bilateral blindness and death. The duration of the cycle was likely to have been 1 year.

Outcomes assessed in the review
The outcomes included:
estimates of the age distribution of ocular hypertension,
the risk of POAG among patients for whom hypotensive medication was and was not prescribed,
the probability of progression of POAG to unilateral blindness,
the probability of bilateral blindness in patients with unilateral blindness,
the impact of POAG and blindness on quality of life, and
mortality.

Side effects were not included because the OHTS did not find any substantive differences between the observation and treatment groups. However, a trend seen in the OHTS for increased cataract extraction in the medication group was modelled.

Study designs and other criteria for inclusion in the review
The review does not appear to have been systematic. The authors did not report the study designs and criteria for inclusion in the review. They seem to have selected studies that reported relevant data.

Sources searched to identify primary studies
The sources searched were not explicitly reported but it was clear that, amongst other things, the authors had used some unpublished data received via personal communication.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
The validity of the primary studies does not appear to have been assessed.

Number of primary studies included
The authors reported six primary studies or references as sources of effectiveness evidence.

Methods of combining primary studies
Data from the primary studies were combined using narrative methods and regression analysis.

Investigation of differences between primary studies
The authors do not appear to have investigated differences between the primary studies.

Results of the review
The annual risk of developing POAG varied from 1.50% in patients aged 40 to 49 years, to 2.69% in patients aged 70 and older (range: +/- 80%).

The reduction in risk of POAG by medical treatment was estimated to be 53% (range: 25 to 65).

The annual probability of progression by one POAG stage was 5.0% (range: 0.005 to 10).

The annual probability of progression from unilateral to bilateral blindness was 1.65% (range: 0.1 to 2.9).

The proportion of patients with an IOP of at least 24 mmHg who met the treatment risk threshold was:
0% in the "Treat no-one" cohort;

100% in the "Treat everyone" cohort;

ranged from 5% (range: 5 to 10; age group 40 - 49 years) to 15% (range: 15 to 30; age group 70+ years) in the "Treat \(\geq 2\%\)" cohort; and

ranged from 22% (range: 22 to 44; age group 40 - 49 years) to 46% (range: 46 to 92; age group 70+ years) in the "Treat \(\geq 5\%\)" cohort.

The increased risk of cataract surgery with treatment was 0.33% (range: 0 to 6.0).

**Measure of benefits used in the economic analysis**

Quality-adjusted life-years (QALYs) were the outcome measure used in the economic analysis. The authors used a mix of published and unpublished data to estimate utility losses for cataract surgery, the five stages of POAG and bilateral blindness. The methods of valuation in the published studies (Brown et al. 2001 and Jampel et al. 2002, see 'Other Publications of Related Interest' for bibliographic details) were not reported here. The unpublished data (for stages 2 to 5 of POAG progression) were collected by investigators at Washington University from 99 people with glaucoma, at urban and suburban clinical settings in the St. Louis area. The authors stated these data were used because they were conservative and that they were collected with standard gamble methodology, implying that the published data were not collected in this way.

**Direct costs**

The future costs and benefits were discounted at a rate of 3% per annum. Most costs and quantities were not analysed separately, and the quantities of resource use were not reported. The costs included weighted average medication costs, office visits, travel to office visits, cataract surgery, treatment of POAG at the various stages, and the costs of glaucoma-related blindness. In the case of the latter two categories, it appears that the direct and indirect costs might have been incorporated together. The authors referred to personal and governmental costs, which may or may not have included indirect costs, despite the statement of a societal perspective. Medication and office visit costs were estimated from clinical trial data (the OHTS), while other costs were taken from published literature. The cost of blindness was taken as the mean of the reports in one review (Lee et al. 2006 and Meads and Hyde, 2003, see 'Other Publications of Related Interest' for bibliographic details). Medication was evaluated at 2005 Medicare average wholesale prices. It was not reported whether other costs were inflated to 2005.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

See the 'Direct Costs' section.

**Currency**

US dollars ($). The costs of blindness were converted from UK sterling at the rate of 1 = $1.8681.

**Sensitivity analysis**

The authors conducted one- and two-way sensitivity analyses using ranges reported in the paper. They also conducted threshold and probabilistic sensitivity analyses. The model was calibrated by conducting a first-order Monte Carlo simulation, re-sampling 10,000 times to estimate the incidence cases of POAG and unilateral and bilateral blindness. Second-order Monte Carlo simulation was conducted, re-sampling 50,000 times to assess the variability of the cost-effectiveness decision. The methods used to select the ranges were not reported, but authors' assumptions appear to
Estimated benefits used in the economic analysis
The total modelled benefits were:

- 13.5370 QALYs in the "Treat no-one" group,
- 13.5588 QALYs (0.0218 incremental QALYs) in the "Treat >/= 5%" group,
- 13.5876 QALYs (0.0288 incremental QALYs) in the "Treat >/= 2%" group, and
- 13.5870 QALYs (-0.0006 incremental QALYs) in the "Treat everyone" group.

Cost results
The total modelled costs were:

- $4,006 in the "Treat no-one" group,
- $4,086 ($80 incremental cost) in the "Treat >/= 5%" group,
- $5,308 ($1,222 incremental cost) in the "Treat >/= 2%" group, and
- $11,245 ($5,937 incremental cost) in the "Treat everyone" group.

Synthesis of costs and benefits
The estimated benefits and costs were combined in incremental cost-utility ratios.

The ratio for the "Treat >/= 5%" group compared with the "Treat no-one" group was $3,670 per QALY gained. The ratio for the "Treat >/= 2%" group compared with the "Treat >/= 5%" group was $42,430 per QALY gained.

The cost-effectiveness frontier excluded the "Treat everyone" group, which was dominated by the "Treat >/= 2%" group (lower costs and higher effectiveness). This was due to the increased risk of cataract surgery associated with treatment.

If it were found that there was no confirmed link between treatment and lens opacities, then the "Treat everyone" option would no longer be dominated, but the resulting incremental cost-effectiveness ratio would be in excess of $1.7 million.

In all sensitivity scenarios, a change in the cost-effectiveness decision resulted in the "Treat >/= 5%" becoming the favoured option.

The decision was sensitive to the incidence of POAG without treatment (threshold value 1.496%), the proportion of people treated (threshold 30%), size of the treatment effect (threshold 30%), cost of medication (threshold $718), and utility loss associated with POAG when correlated with Stage 1 (threshold 0.0132).

The Monte Carlo simulation showed that at willingness-to-pay thresholds beyond $43,000 per QALY, "Treat >/= 2%" is more likely to be the most cost-effective treatment threshold. Below $43,000 per QALY, "Treat >/= 5%" is more likely to be preferred.

Authors' conclusions
The treatment of high-risk patients (2% or 5% annual risk of primary open-angle glaucoma) with an intraocular pressure (IOP) of at least 24 mmHg was highly cost-effective and should give confidence to clinicians to recommend
medical treatment to those with risk factors who have a preference for avoiding progression of their disease. The findings support a decision not to treat patients at lower risk if the patient and clinician agree that health status and expected longevity make "watchful waiting" preferable.

CRD COMMENTARY - Selection of comparators
The justification for the comparative treatment thresholds in the model was the precision of available estimates of risk. The authors selected thresholds of 2% and 5% annual risk as having a reasonable separation and being as inclusive as possible to maximise the social benefit gained. Various strategies of treatment were compared, rather than the actual treatments themselves. You should decide if these options represent reasonable comparators in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. They used data from the available studies selectively, but considered the impact of differences between the primary studies when selecting and including data and through the sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of benefits (QALYs) was modelled using a mixture of American and British utility data. The instruments used to derive measures of benefit appear to have been appropriate. The measure enables broad comparisons to be made with other technologies.

Validity of estimate of costs
A societal perspective was adopted but, because the costs and quantities were not sufficiently separated, it is difficult to confirm that indirect costs were in fact included. Similarly, it is difficult to confirm that all the relevant costs for each category were included, or whether omissions are likely to affect the conclusions. The costs of adverse effects of treatment were discussed, but not included, because they were not expected to be significant (apart from a potential link to increased cataract surgery). Resource use was extracted from published studies and unpublished data from a clinical trial (medication quantities). A sensitivity analysis was conducted on the costs, though the ranges used were not justified. The medication quantities were not varied directly. The prices were taken from dated published sources; a sensitivity analysis was conducted on average medication costs. The authors performed an appropriate currency conversion and discounting.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and explored the drivers and assumptions within their model extensively. The issue of generalisability to other settings was not addressed, except with reference to national willingness-to-pay thresholds. The authors presented their results comprehensively and their conclusions reflected the scope of the analysis.

The authors addressed some potential limitations in the model. First, the effectiveness estimate was based on a treatment strategy rather than a specific medication protocol, which the authors believe will reduce the distortion in effect between clinical trial settings and generalisation to clinical practice. Second, based on recent studies, it is likely that the true incidence of POAG among patients with an IOP of at least 24 mmHg is higher than the estimate included in the model. Finally, depending on the characterisation of progression, it is possible that the model overestimated the speed of POAG in the base-case. However, the sensitivity analysis showed that the results held, even for much lower rates of POAG progression.

Implications of the study
The authors noted that utility loss associated with POAG and progression rates of POAG were among the most influential variables in the model. They suggested that further investigation would provide important information on the evaluation of treatments to prevent or slow glaucoma. Present risk models for the progression to POAG do not describe
the precision of their estimates of risk, and so must be viewed with caution in characterising risk for the individual patient. However, the authors stated that, on average, the results of the model show that treatment is likely to be cost-effective in high-risk groups, and that delaying treatment to anyone other than patients with the lowest risk of progression is not likely to represent an efficient use of society's resources.

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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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