Clinical and economic impact of new trends in glaucoma treatment
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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.

Health technology
This study considered the implications of first-line treatment of primary open-angle glaucoma with brimonidine 0.2% (an adrenergic agent second-generation alpha2-agonist) and betaxolol 0.25% (a selective adrenergic beta-blocker). For both drugs the dosing regimens was 1 drop per eye, twice daily.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged at least 21 years with newly diagnosed or untreated ocular hypertension, or primary open-angle glaucoma with intraocular pressure (IOP) of 34 mmHg or less in each eye and asymmetrical pressure of 5 mmHg or less, and corrected visual acuity of 20/100 or greater in each eye. Patients were excluded from the population if they had an uncontrolled systemic disease, or known allergy or sensitivity to either drug. They were also excluded if they had an abnormal heart rate, blood pressure, or any contraindication to the study comparators.

Setting
The setting was primary and secondary care. The paper did not explicitly report the geographical setting of the study, although it appears to have been carried out in the USA.

Dates to which data relate
The clinical effectiveness data were taken from a study published in 2000. The resource use data were modelled using the same information. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a published study (Javitt et al. 2000, see 'Other Publications of Related Interest' for bibliographic details).

Study sample
The authors reported a few details on the study sample, as obtained from the published parent study (Javitt et al. 2000, see 'Other Publications of Related Interest' for bibliographic details). A total of 188 patients were included in the analysis, but the numbers allocated to each treatment were not reported. The paper did not include any sample size or power calculations.
Study design
The study was a multi-centre, double-blind randomised trial. The authors did not give any details of the centres included in the study or how the patients were randomised. The patients were followed up for 4 months. The duration of follow-up varied between 1 week and 5 months if the patients did not achieve clinical success with the primary treatment choice. The number of patients lost to follow-up was not specified.

Analysis of effectiveness
The analysis of the clinical study appears to have been conducted for treatment completers only. The primary outcome assessed in this study was clinical success. Clinical success rate was defined as the likelihood of drug continuation following the initial assessment. It was expressed in the disease intervention model as a probability. Clinical success encompassed several measures. For example, reduction in IOP, quality of life effects based on Glaucoma Disability Index scores, and adverse events. Therefore, the decision to continue treatment was based on all of the measures stated above. At week 1 (an optional visit) and at month 1, the study patients were evaluated to determine whether they should continue on the assigned medication or change to the alternative study drug. Study patients still on the initial medication at month 4 (the exit visit) were assessed to determine clinical success (i.e. whether they should continue on their current treatment when the study concluded). The two groups were not compared at baseline.

Effectiveness results
The rate of clinical success was 73.9% (65 out of 88) in the brimonidine group and 56.2% (51 out of 91) in the betaxolol group, (p=0.027).

No significant difference between treatment groups was noted in the mean change from baseline in Glaucoma Disability Index summary scores at any follow-up visit.

There was no statistically significant difference in the number of patients reporting adverse events. However, ocular blurring was reported more often in the betaxolol group than in the brimonidine group, (p=0.027).

Clinical conclusions
The authors concluded that brimonidine 0.2% has a greater clinical efficacy than betaxolol 0.25%.

Modelling
A decision tree model was used to assess the resource use associated with the two treatments. The model extended the 4-month time span of the study to a year and added the impact of additional treatments. The authors reported that the model was modified to mimic real world circumstances, but did not give any details of these alterations. A 50% (even odds) success rate was assumed for third-, fourth- and fifth-line therapies, and was applied equally along appropriate decision tree branches for both comparators.

Measure of benefits used in the economic analysis
No summary measure of benefits was produced, the measure of health benefit being clinical success. In effect, the authors carried out a cost-consequences analysis.

Direct costs
The estimate of the resources used was derived from the decision tree model. The direct costs of the health care provider were assessed. According to the authors, the costs included in the analysis were for medications, ophthalmologist visits (with a distinction made between an initial and a follow-up visit), treatment of adverse events, and surgery (argon laser trabeculoplasty). The unit costs of drugs were taken from the Red Book, while the unit costs of physician visits and surgery were taken from the Medicare Fee Schedule. The resource use data and the unit costs were not consistently reported separately. No price year or date for the resource use data was given. Discounting was not relevant and was not carried out.
Statistical analysis of costs
The cost data were treated deterministically. No statistical analysis of the costs was carried out.

Indirect Costs
No indirect costs were included in the study.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was undertaken to assess the robustness of the study findings. A rank order stability analysis was also undertaken, but the authors did not report whether this was a one-way or multi-way analysis. The variables were varied to find the point at which the more cost-effective treatment changed.

Estimated benefits used in the economic analysis
The rate of clinical success in the two patient groups has been reported already (see Effectiveness Results). The duration of the benefits was extended in the decision tree model to one year.

Cost results
The total cost was $301.37 for first-line treatment with brimonidine, compared with $328.19 when betaxolol was used as the first line of treatment.

Synthesis of costs and benefits
The cost-effectiveness of first-line treatment with brimonidine was $407.70 per clinical success, compared with $583.86 per clinical success with betaxolol.

The sensitivity analysis found that reasonable changes in the efficacy rate, the cost of the two drugs and the cost of full medical management did not alter the conclusions.

Authors' conclusions
Brimonidine is a more clinically and cost-effective first-line therapy than betaxolol in patients with primary open-angle glaucoma.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was justified. Betaxolol is a type of topical beta-blocker, and the authors considered beta-blockers to be the most commonly used drugs to treat primary open-angle glaucoma. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The clinical effectiveness data used in this study were taken from a multi-centre randomised trial. This had the potential to provide a very robust assessment of the effectiveness of the two interventions. However, the paper did not include any information on the method of randomisation, thus the potential for bias in this area cannot be assessed. Further, the analysis of the results appears to have been for treatment completers only since the final sample size considered in the analysis (n=179) was less than the initial sample size (n=188), although the authors did not clearly state as much. This will provide an overestimate of the true effectiveness of the treatment in a real world setting.
The authors did not compare their study sample with the study population. It is therefore not possible to assess whether the study sample was representative of the study population. In addition, no comparison of the baseline characteristics of two patient groups was reported. This means that it is not possible to identify whether differences in the two patients groups could have accounted for the differing effectiveness of the two drugs. Another drawback of the study was that there was no statistical analysis of the health outcomes. These facts limit the internal validity of the study.

**Validity of estimate of measure of benefit**
Clinical success was used as the measure of benefit in the economic analysis. Clinical success was judged using a combination of efficacy, changes in quality of life and adverse events. It was not entirely clear how this was judged, but it appears to have been partially subjective. In addition, the assumption of a 50% success rate for third-, fourth- and fifth-line therapies was not justified based on the literature.

**Validity of estimate of costs**
The paper did not explicitly report the economic perspective used, although a health care provider view appears to have been adopted. The authors provided insufficient detail of the cost analysis and it is unclear whether the cost analysis was handled credibly. The paper did not provide a breakdown of the resource use data and the unit costs. This limits the scope in applying the findings to other settings. The resource use quantities were taken from a single study and were extrapolated using the decision tree model. There was no statistical or sensitivity analysis of the quantities, and no other source was used for the resource quantities. No price year was reported, which will prevent any further reflation exercises to enable comparisons with other studies. On the other hand, an appropriate sensitivity analysis was undertaken to assess variability in efficacy and the costs. This showed the robustness of the study conclusions. Discounting was, appropriately, not undertaken since all of the costs were incurred during less than two years.

**Other issues**
The authors did not compare their findings with other studies, nor did they explicitly consider how they could be generalised to other settings. The authors did not present their results selectively and their conclusions reflected the data presented in the paper. However, a more comprehensive presentation of the data would have clarified a number of issues. The authors did not report any further limitations of their study.

**Implications of the study**
The authors did not make any specific recommendations for further research or changes in practice.

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**Other publications of related interest**

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