A Markov modelled pharmacoeconomic analysis of bimatoprost 0.03% in the treatment of glaucoma as an alternative to filtration surgery in Italy

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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
The authors investigated the use of bimatoprost 0.03% as an alternative to filtration surgery (FS) in the treatment of glaucoma. Patients treated on bimatoprost began treatment with bimatoprost, but proceeded to FS if the target intraocular pressure (IOP) was not reached using medical therapy. Patients in the surgery group received surgery after the first ophthalmologist visit.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of glaucoma patients on MTMT. All patients were scheduled for surgery because of inefficacy of the MTMT and/or progressive deterioration of the visual field.

Setting
The study setting was secondary care. The economic study was undertaken in Italy.

Dates to which data relate
The effectiveness data were derived from a study published in 2005. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a single study (Vertugno et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). These data were supplemented with estimates from a Delphi panel of Italian ophthalmologists.

Link between effectiveness and cost data
The resource data were obtained from both the clinical study population and Delphi panel estimates.

Study sample
The effectiveness data were derived from a single study (Vertugno et al. 2005), of which only brief details were presented. A total of 83 patients were recruited from the waiting list for glaucoma surgery.
**Study design**
The study was an RCT. The patient groups appear to have been followed for 3 months. The authors only reported limited information on the study design, referring instead to the parent clinical paper (Vertugno et al. 2005).

**Analysis of effectiveness**
The health outcomes used in the analysis were the stage-specific transition probabilities used in the Markov model and the proportion of patients who delayed the need for FS.

**Effectiveness results**
The probability of remaining on bimatoprost monotherapy was 72.3% after the first month and 90.0% after the third month.

The probability of changing from monotherapy to combo-therapy was 4.8% after the first month and 10.0% after the third month.

The probability of changing from monotherapy to surgery was 22.9% after the first month and 0.0% after the third month.

The probability of remaining on combo-therapy was 0.0% after the first month and 50.0% after the third month.

The probability of changing from combo-therapy to surgery was 0.0% after the first month and 50.0% after the third month.

The probabilities of post-surgery with and without beta-blocker added were 0.0% after the first month and third month.

The trial showed that 74.7% of the patients in the bimatoprost group delayed the need for FS by 3 months.

**Clinical conclusions**
The authors concluded that bimatoprost could represent a useful therapeutic tool that might defer FS.

**Modelling**
A decision-analytic model, including a Markov model, was used to extrapolate the results of the clinical study beyond the time horizon of the randomised controlled trial. Based on this model, a cost-minimisation analysis was conducted. The model used monthly cycles and continued for up to 4 years (48 months). Stage-specific transitions of the Markov model were as follows:

- remain on bimatoprost monotherapy;
- change from monotherapy to combo-therapy;
- change from monotherapy to surgery;
- remain on combo-therapy;
- change from combo-therapy to surgery;
- post-surgery without beta-blocker added; and
- post-surgery with beta-blocker added.

Sub-group analyses were also performed to obtain relevant transition probabilities from groups with less than 20% IOP reduction, 20 to 30% IOP reduction, and more than 30% IOP reduction.
Methods used to derive estimates of effectiveness
The effectiveness data from the RCT were supplemented with estimates from a Delphi panel of Italian ophthalmologists, in which experts established and obtained consensus. According to the authors, all 8 ophthalmologists had large experience of FS and glaucoma management. The experts were asked to extrapolate the stage-specific transition probabilities of bimatoprost therapy and FS.

Estimates of effectiveness and key assumptions
The following stage-specific transition probabilities were derived from the Delphi panel.

The probability of remaining on bimatoprost monotherapy was 90.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of changing from monotherapy to combo-therapy was 10.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of changing from monotherapy to surgery was 0.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of remaining on combo-therapy was 50.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of changing from combo-therapy to surgery was 50.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of post-surgery without beta-blocker added was 99.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

The probability of post-surgery with beta-blocker added was 1.0% after 6, 12, 18, 24, 30, 36, 42 and 48 months.

Measure of benefits used in the economic analysis
The measure of benefits used was the proportion of patients with delayed need for FS after 4 years. This was derived directly from the model.

Direct costs
The direct costs included in the analysis were those to the health care sector. These were for visits to the ophthalmologist, FS, beta-blockers (timolol 0.50%) and bimatoprost. The resource use data were derived from the trial by Vertugno et al. (2005) and by the Delphi panel. The unit costs for ophthalmologist visits and surgery were derived from chart and tariffs reviews, whereas the costs of drugs were derived from an Italian pharmacy website. Since the costs could be incurred during a 4-year period, all future costs were appropriately discounted using an annual rate of 3%, as recommended by Italian guidelines for economic evaluations. The study reported the average costs. All costs were reported in 2002 prices.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The authors reported that the glaucoma patients considered in this study were old (mean age 66 years in the study by Vertugno et al. 2005). Consequently, lost productivity due to the disease may be close to zero. Therefore, the authors considered that the indirect costs would not be relevant.

Currency
Euros (EUR).
Sensitivity analysis
The authors performed several sensitivity analyses. For example, using different timeframes for the analysis, and estimating the consequences upon the costs if 5% more patients remained on bimatoprost monotherapy instead of combo-therapy or FS. The effects of decreasing the effectiveness of bimatoprost by 20% and not discounting the costs were also investigated in sensitivity analyses.

Estimated benefits used in the economic analysis
The model estimated that 64.2% of patients delayed the need for surgery after 1 year, 53% delayed the need for surgery after 2 years, and after 4 years 34.9% of patients had avoided FS.

Cost results
After 4 years, the costs in the bimatoprost arm were 19.6% lower than FS (EUR 3,438 versus EUR 4,194, with an incremental cost of EUR 755).

Synthesis of costs and benefits
The costs and benefits were not combined.

The results of the sensitivity analysis showed that if 5% more patients remained on bimatoprost monotherapy during the 4 years, the costs of the MTMT alternative decreased to EUR 3,008. When decreasing the effectiveness of bimatoprost by 20%, the number of patients avoiding FS decreased, with 11.5% of patients avoiding surgery after 4 years, and bimatoprost also being less costly than surgery. When a 0% discount rate was used, the difference in costs decreased.

Authors' conclusions
Bimatoprost was cheaper than filtration surgery (FS).

CRD COMMENTARY - Selection of comparators
A justification was given for using FS as the comparator. A filtration procedure is recommended when the progression of glaucoma in patients on MTMT has been insufficiently controlled. You should decide if this intervention is current practice in your own settings.

Validity of estimate of measure of effectiveness
The effectiveness data were derived mainly from an RCT. This was appropriate for the study question as well-conducted RCTs are considered the 'gold' standard study design when comparing health interventions. However, the authors provided very few details of this trial in their article, thus it was difficult to ascertain the internal validity of the clinical study. The effectiveness data from the trial were supplemented by expert opinion, which was elicited from a Delphi panel of 8 Italian ophthalmologists when data from the RCT were insufficient. The authors reported that the panel had large clinical experience of FS and glaucoma management. Limited sensitivity analyses were undertaken on the effectiveness parameters of bimatoprost.

Validity of estimate of measure of benefit
The authors reported that they conducted a cost-minimisation analysis. However, they showed that bimatoprost was effective at delaying surgery, which could be considered a benefit. The authors estimated the proportion of patients who delayed surgery over a 4-year period using a Markov model, which was appropriate for the study question.

Validity of estimate of costs
All the cost categories relevant to the health care system perspective were included in the analysis. The costs related to home and institutional care were not included, although relevant given the age of the patients. However, the authors
reported that it was not expected that these costs, being present in both groups, would have changed the results. Although the authors did not report the costs and the quantities separately, they reported all unit costs used in the analysis together with their sources, which will increase the generalisability of their results. The resource use data were derived from the RCT and expert opinion from the Delphi Panel. The unit costs were derived from chart and tariff reviews, whilst the drug costs were derived from the Italian pharmacy website. Charges were used to proxy prices; hence the true cost of the interventions may not be reflected in the analysis. Limited sensitivity analyses of the costs were undertaken. Since the costs were incurred during a 4-year period, all future costs were appropriately discounted. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors reported that another large study had found that bimatoprost could represent a useful therapeutic tool for deferring FS. The issue of generalisability to other settings was partly addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, the decision analytic model was based solely upon clinical evidence from one RCT, as well as a Delphi panel. Second, the costs related to home and institutional care were not included, although relevant given the age of the patients.

Implications of the study
The authors reported that the postponement of FS associated with bimatoprost may have important implications for waiting-list planning.

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Bibliographic details
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Other publications of related interest


Indexing Status
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MeSH
Aged; Amides; Bimatoprost; Cloprostenol /analogs & derivatives; Cost-Benefit Analysis; Filtering Surgery /economics; Glaucoma /drug therapy /economics /surgery; Health Care Costs; Humans; Intraocular Pressure /drug effects /physiology; Italy; Lipids /economics /pharmacology /therapeutic use; Markov Chains; Ophthalmic Solutions