A cost-effectiveness comparison of bimatoprost versus latanoprost in patients with glaucoma or ocular hypertension

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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 use of bimatoprost 0.03% QD (BIM) and latanoprost 0.005% QD (LAT) in patients with glaucoma or ocular hypertension (OHT). The drugs were administered into both eyes once daily, in the evening.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with a diagnosis of OHT or glaucoma, and an intraocular pressure (IOP) of >= 22 and <= 34 mmHg in at least one eye. Patients were excluded if they had any condition or medication that would put them at risk during the course of the study, or interfere with interpretation of the study results. Also excluded were patients with any sensitivity or contraindication to the study medication. Women who were pregnant, nursing, or of childbearing potential who were not using a reliable form of contraception, were also excluded.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 2001 and 2003. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A simple decision tree structure was used to define the treatment algorithm. Patients visited a physician at baseline and were prescribed one of the two first-line treatments. Patients had a follow-up visit at 1 month and another after 3 months. Those who achieved lower IOP levels were kept on their first-line treatment and were then visited at month 9. For those who failed to achieve lower IOP levels, the physicians prescribed adjunctive medication (dual therapy) and the patients were visited at months 4, 6 and 12. Therefore, the time horizon of the mathematical model (algorithm) was 1 year.
Outcomes assessed in the review
The outcomes estimated from the literature were:

- the proportions of patients achieving target pressures at 12 pm after 3 months and after 6 months of follow-up; and
- the percentage of patients in which physicians wanted to reach specific target IOPs.

Study designs and other criteria for inclusion in the review
A systematic review of the literature does not appear to have been undertaken. Two clinical trials (follow-up of 3 and 6 months, respectively) and an unpublished 361-patient, nationwide, internet-based research survey (involving physicians randomly selected from 32 centres throughout the US) were used as primary sources.

Sources searched to identify primary studies
Not stated.

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

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Three primary studies provided the evidence.

Methods of combining primary studies
The primary estimates appear to have been combined using a narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
The proportions of patients achieving target pressures at 12 pm after 3 months were:

- 10% with BIM and 3% with LAT, (p=0.049) for levels of <= 13 mmHg,
- 19% (BIM) and 8% (LAT), (p=0.038) for levels of <= 14 mmHg,
- 29% (BIM) and 14% (LAT), (p=0.009) for levels of <= 15 mmHg,
- 45% (BIM) and 35% (LAT) for levels of <= 16 mmHg, and
- 58% (BIM) and 50% (LAT) for levels of <= 17 mmHg.

The proportions of patients achieving target pressures at 12 pm after 6 months were:

- 14% with BIM and 6% with LAT, (p=0.040) for levels of <= 13 mmHg,
- 21% (BIM) and 11% (LAT), (p=0.030) for levels of <= 14 mmHg.
36% (BIM) and 22% (LAT), \( (p=0.015) \) for levels of \( \leq 15 \text{ mmHg} \),
51% (BIM) and 38% (LAT), \( (p=0.027) \) for levels of \( \leq 16 \text{ mmHg} \),
65% (BIM) and 45% (LAT), \( (p=0.001) \) for levels of \( \leq 17 \text{ mmHg} \),
70% (BIM) and 60% (LAT), \( (p=0.125) \) for levels of \( \leq 18 \text{ mmHg} \),
82% (BIM) and 71% (LAT), \( (p=0.044) \) for levels of \( \leq 19 \text{ mmHg} \), and
91% (BIM) and 79% (LAT), \( (p=0.010) \) for levels of \( \leq 20 \text{ mmHg} \).

The percentages of patients in which physicians wanted to reach specific target IOPs were:

- 13% for levels of \( \leq 13 \text{ mmHg} \),
- 11% for levels of \( \leq 14 \text{ mmHg} \),
- 19% for levels of \( \leq 15 \text{ mmHg} \),
- 16% for levels of \( \leq 16 \text{ mmHg} \),
- 16% for levels of \( \leq 17 \text{ mmHg} \),
- 12% for levels of \( \leq 18 \text{ mmHg} \),
- 2% for levels of \( \leq 19 \text{ mmHg} \), and
- 11% for levels of \( \leq 20 \text{ mmHg} \).

Measure of benefits used in the economic analysis

The summary benefit measure was the success rate (proportion of patients who achieved target pressures at 12 pm) associated with BIM and LAT after one year of treatment. The success rate was derived from the effectiveness analysis using 6-month rates that were extrapolated to 1 year of follow-up, supported by evidence that BIM or LAT efficacy did not vary substantially from 6 to 12 months.

Direct costs

Discounting was not relevant since the costs were incurred during 1 year. The unit costs were presented separately from the quantities of resources used. The health services included in the economic evaluation were BIM and LAT, (both used as first- or second-line treatment), and both initial and subsequent outpatient visits. The cost/resource boundary of the study appears to have been that of an MCO. Resource use was estimated using treatment patterns developed by a panel of 8 glaucoma experts. The drug costs were derived from average wholesale prices, while the costs of patient visits were estimated from the Physician Fee and Coding Guide. The price year was 2003.

Statistical analysis of costs

The costs were treated deterministically.

Indirect Costs

The indirect costs were not included in the economic evaluation.

Currency
US dollars ($).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to determine the impact of changes in the drug costs and success rates on the estimated cost-effectiveness ratios.

**Estimated benefits used in the economic analysis**
See the ‘Effectiveness Results’ section.

**Cost results**
The total costs associated with BIM and LAT were quite comparable. The total expected costs were, respectively:

- $1,238 (BIM) and $1,257 (LAT) for a target IOP of <= 13 mmHg,
- $1,181 (BIM) and $1,224 (LAT) for a target IOP of <= 15 mmHg,
- $1,093 (BIM) and $1,115 (LAT) for a target IOP of <= 17 mmHg, and
- $1,005 (BIM) and $1,018 (LAT) for a target IOP of <= 20 mmHg.

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the two treatment options.

The average costs per treatment success with BIM and LAT were, respectively:

- $8,845 (BIM) and $20,954 (LAT) for a target IOP of <= 13 mmHg,
- $3,280 (BIM) and $5,563 (LAT) for a target IOP of <= 15 mmHg,
- $1,681 (BIM) and $2,447 (LAT) for a target IOP of <= 17 mmHg, and
- $1,104 (BIM) and $1,288 (LAT) for a target IOP of <= 20 mmHg.

The average cost-effectiveness ratio with BIM was 58% lower than that with LAT for a target IOP of <= 13 mmHg, 41% for a target IOP of <= 15 mmHg, 32% for a target IOP of <= 17 mmHg, and 14% for a target IOP of <= 20 mmHg.

The incremental analysis revealed that BIM dominated LAT at any target level because they had similar costs, but BIM was more effective, resulting in a negative incremental cost-effectiveness ratio.

The cost-effectiveness ratios were sensitive to changes in the success rates. However, the success rate of LAT would have to be at least 15 to 133% higher than that of BIM for LAT to be at least as cost-effective as BIM.

The impact of changes in the drug prices was less relevant since the acquisition price of LAT was very close to that of BIM.

**Authors’ conclusions**
Bimatoprost (BIM) was more cost-effective than latanoprost (LAT) over a range of clinically relevant target intraocular pressures (IOPs). The study showed that the difference in cost-effectiveness was most apparent at the lowest target IOPs.
CRD COMMENTARY - Selection of comparators
The selection of the comparators appears to have been appropriate since both were widely used for the treatment of glaucoma and OHT. The dosages and treatment patterns were clearly reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a synthesis of published studies. However, it appears that a systematic review of the literature has not been undertaken and the primary studies were likely to have been identified selectively. The bulk of the evidence came from randomised clinical trials, which should ensure a high internal validity. The issue of the comparability of the sources used was not addressed. Uncertainty around the estimators was not investigated in the sensitivity analysis. Target IOP levels were used as a proxy for progression to blindness. Several levels (mmHg) were considered and the validity of the outcome measure was assured by a survey of clinical experts.

Validity of estimate of measure of benefit
The summary benefit measure was obtained directly from the effectiveness evidence, assuming that the benefits estimated after 6 months could be extrapolated to a 1-year time horizon. This assumption was based on published data. The impact of variations in the success rate was investigated in the sensitivity analysis. The use of success rate as a summary benefit measure does not permit comparisons to be made with the benefits of other health care interventions.

Validity of estimate of costs
The authors did not state explicitly which perspective was adopted in the study, although it appears that costs relevant to the payer (i.e. a MCO) have been included in the analysis. The unit costs were presented separately from quantities of resource used. Consequently, the analysis is easily replicated in other contexts. The cost estimates were specific to the study setting and statistical analyses were not carried out on the costs. The source of the data was reported. Resource consumption was derived from experts’ assumptions and such estimates were not tested in the sensitivity analysis. The price year was reported, which aids reflation exercises in other settings. The authors noted that the costs associated with the surgical treatment of glaucoma were not considered in the treatment algorithm, as these would have added substantial expenses to the failure branches of the tree and thus affected, proportionately, the two treatments. The authors acknowledged that the treatment of side effects related to medical treatment was not accounted for in the analysis.

Other issues
The authors did not make extensive comparisons of their findings with those from other pharmacoeconomic studies. They also did not explicitly address the issue of the generalisability of the results of the analysis to other settings. The use of sensitivity analysis was quite limited since only a few model inputs were investigated. This affected the external validity of the study. The issue of treatment compliance was not explicitly addressed, although it could have been examined in the primary trials. The authors acknowledged that the time horizon of the analysis could have been too short to capture all the benefits and costs of the treatment options. However, this was due to the lack of long-term reliable data.

Implications of the study
The study results suggested that BIM dominated LAT as IOP-lowering treatment in patients with glaucoma or OHT.

Source of funding
None stated.

Bibliographic details

**PubMedID**
15016560

**DOI**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Algorithms; Amides; Antihypertensive Agents /economics; Bimatoprost; Cloprostenol /analogs & derivatives; Cost-Benefit Analysis; Drug Costs; Economics, Pharmaceutical; Glaucoma, Open-Angle /economics; Health Care Costs; Humans; Intraocular Pressure /drug effects; Lipids /economics; Ocular Hypertension /economics; Prostaglandins F, Synthetic /economics

**AccessionNumber**
22004000546

**Date bibliographic record published**
30/04/2005

**Date abstract record published**
30/04/2005