An economic analysis of switching to latanoprost from a beta-blocker or adding brimonidine or latanoprost to a beta-blocker in open-angle 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 authors investigated a switch to latanoprost monotherapy, or the addition of latanoprost or brimonidine, for patients with ocular hypertension or primary open-angle glaucoma that was uncontrolled on beta-blocker therapy alone.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was drawn from patients attending large glaucoma practices in Charleston (SC) and Atlanta (GA), who had been prescribed a topical beta-adrenergic blocker as monotherapy and were then switched to latanoprost (0.005% once daily), or had either brimonidine (0.2% twice daily) or latanoprost (0.005%) added to the beta-blocker therapy. The patients must also have had at least one follow-up visit after the change in therapy. To be included in the study, the patients were required to be at least 18 years of age, and to have a clinical diagnosis of open-angle glaucoma or ocular hypertension in at least one eye. They also had to have received one of the treatment strategies described above.

The authors reported that patients were excluded from the study if they had an abnormality that prevented reliable applanation tonometry in the study eye(s), or media opacity preventing reliable baseline optic nerve or visual field evaluation. They were also excluded if they had undergone intraocular conventional surgery or laser surgery within 3 months of the change in beta-blocker therapy. Also excluded were those with a diagnosis of primary acute or chronic angle closure, or secondary as well as congenital glaucoma, known occludable angles by gonioscopy, and the presence of any other clinically significant known angle abnormality. Patients using more than one other glaucoma medicine at the baseline visit were also excluded.

Setting
The practice setting appears to have been the offices of ophthalmologists with large glaucoma practices in Charleston (SC) and Atlanta (GA), USA. The economic study was carried out in the USA.

Dates to which data relate
It would appear that the effectiveness evidence was collected between 1996 and January 2001. The dates for the resource use data were not reported. The prices used were derived from 2001 publications.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
The authors did not report the use of power calculations (either prospectively or retrospectively). However, they did report that the study had to have at least 37 patients enrolled in each treatment group and that, if necessary, up to a 2:1:1 admission ratio was allowed. The sample was selected by accessing consecutive (alphabetical or numerical) patient records. The authors did not justify their choice of sample with respect to the clinical question. However, the sample inclusion and exclusion criteria appear to have been quite stringent, which would suggest that the study sample was appropriate for the clinical question. The study sample was made up of 37 patients who received latanoprost monotherapy, 74 who received latanoprost plus a beta-blocker, and 37 who received brimonidine plus a beta-blocker.

Study design
This was a multi-centred, retrospective cohort study. The number of centres was not reported. The authors had planned an exact 12-month follow-up period, but this was not possible for all patients. Loss to follow-up was not reported. It should be noted that the time on the study treatment (mean +/- standard deviation, SD) was 10.6 (+/- 4.3) months for the latanoprost monotherapy group, 11.2 (+/- 3.7) months for the latanoprost plus beta-blocker group, and 9.4 (+/- 4.9) months for the brimonidine plus beta-blocker group, (p=0.1). The time in the study (mean +/- SD) was 11.6 (+/- 3.7) months for the latanoprost monotherapy group, 12.1 (+/- 3.0) months the latanoprost plus beta-blocker group, and 11.2 (+/- 4.5) months for the brimonidine plus beta-blocker group, (p=0.45).

Analysis of effectiveness
The authors reported that, because not all patients had a follow-up period that was exactly 12 months in length, the analysis of costs, visits and medicine changes were assessed on a per month basis. Efficacy results are given for values observed at the final follow-up visit and for the last on-study-treatment visit. The primary health outcomes used in the analysis were:

- intraocular pressure (IOP),
- the number of medicine changes per month during the follow-up time,
- the average number of visits per person per month, and
- the total number of visits and the number of patients who had a change in therapy to control IOP.

It was reported that no statistical differences were found between the treatment groups in terms of age, gender, race, or beta-blocker prescribed. However, statistical differences between the groups were noted in both the treated eye, (p=0.034), and the study eye, (p=0.018).

Effectiveness results
At baseline, when all patients were receiving beta-blocker alone, there was no statistical difference between the treatment groups.

The IOP (mean +/- SD mmHg) at baseline was 20.9 (+/- 4.9) for the latanoprost monotherapy group, 20.9 (+/- 4.3) for the latanoprost plus beta-blocker group, and 21.7 (+/- 6.3) for the brimonidine plus beta-blocker group, (p=0.71).

The IOP (mean +/- SD) at last on-study-treatment visit (final follow-up visit) was 18.0 +/- 3.0 (18.0 +/- 2.9) for the latanoprost monotherapy group, 16.5 +/- 3.8 (16.4 +/- 4.0) for the latanoprost plus beta-blocker group, and 17.8 +/- 4.4 (17.1 +/- 4.1) for the brimonidine plus beta-blocker group, (p=0.078 (p=0.076)).

The IOP change (mean +/- SD) from baseline to last on-study-treatment visit (final follow-up visit) was 2.9 +/- 5.1 (2.8
(+/- 4.6) for the latanoprost monotherapy group, 4.4 (+/- 5.1) for the latanoprost plus beta-blocker group, and 3.9 (+/- 5.5) for the brimonidine plus beta-blocker group, (p=0.38 (p=0.23)).

The number of medicine changes per person per month (mean +/- SD) were 0.01 (+/- 0.03) for the latanoprost monotherapy group, 0.04 (+/- 0.06) for the latanoprost plus beta-blocker group, and 0.04 (+/- 0.06) for the brimonidine plus beta-blocker group, (p=0.001).

The number of visits per person per month (mean +/- SD) was 0.01 (+/- 0.06) for the latanoprost monotherapy group, 0.04 (+/- 0.06) for the latanoprost plus beta-blocker group, and 0.04 (+/- 0.06) for the brimonidine plus beta-blocker group, (p=0.05).

The total number of visits (mean +/- SD) was 3.8 (+/- 2.0) for the latanoprost monotherapy group, 4.2 (+/- 1.5) for the latanoprost plus beta-blocker group, and 4.5 (+/- 2.0) for the brimonidine plus beta-blocker group, (p=0.16).

Adverse events are detailed below,

There were 10 (27%) incidents of blurred vision in the latanoprost monotherapy group, 15 (20%) in the latanoprost plus beta-blocker group, and 12 (32%) in the brimonidine plus beta-blocker group, (p=0.62).

There were 4 (11%) incidents of allergy in the latanoprost monotherapy group, 16 (22%) in the latanoprost plus beta-blocker group, and 8 (22%) in the brimonidine plus beta-blocker group, (p=0.35).

There were 5 (14%) incidents of tearing or watering in the latanoprost monotherapy group, 9 (12%) in the latanoprost plus beta-blocker group, and 12 (32%) in the brimonidine plus beta-blocker group, (p=0.27).

There were 4 (11%) incidents of conjunctival hyperemia in the latanoprost monotherapy group, 10 (14%) in the latanoprost plus beta-blocker group, and 3 (8%) in the brimonidine plus beta-blocker group, (p=0.69).

There were 3 (8%) incidents of burning or stinging in the latanoprost monotherapy group, 2 (3%) in the latanoprost plus beta-blocker group, and 5 (14%) in the brimonidine plus beta-blocker group, (p=0.095).

There were 3 (8%) incidents of mucus or runny discharge in the latanoprost monotherapy group, 2 (3%) in the latanoprost plus beta-blocker group, and 4 (11%) in the brimonidine plus beta-blocker group, (p=0.095).

There was 1 (3%) incident of blepharitis in the latanoprost monotherapy group, 5 (7%) in the latanoprost plus beta-blocker group, and 2 (5%) in the brimonidine plus beta-blocker group, (p=0.67).

There were 2 (5%) incidents of ocular pain in the latanoprost monotherapy group, 3 (4%) in the latanoprost plus beta-blocker group, and 3 (8%) in the brimonidine plus beta-blocker group, (p=0.67).

The number of incidents of foreign body sensation was "not reported" for the latanoprost monotherapy group, 5 (7%) for the latanoprost plus beta-blocker group, and 2 (5%) for the brimonidine plus beta-blocker group, (p=0.28).

There were 3 (8%) incidents of dryness in the latanoprost monotherapy group, 1 (1%) in the latanoprost plus beta-blocker group, and 1 (3%) in the brimonidine plus beta-blocker group, (p=0.17).

The number of incidents of irritated lids was 1 (3%) in the latanoprost monotherapy group, 2 (3%) in the latanoprost plus beta-blocker group, and "not reported" for the brimonidine plus beta-blocker group, (p=0.60).

The total number of adverse events was 36 for the latanoprost monotherapy group, 70 for the latanoprost plus beta-blocker group, and 52 for the brimonidine plus beta-blocker group.

The total number of patients having adverse events was 21 (57%) for the latanoprost monotherapy group, 41 (55%) for the latanoprost plus beta-blocker group, and 22 (59%) for the brimonidine plus beta-blocker group, (p=0.79).

Clinical conclusions
The study suggests that, for patients who are uncontrolled on beta-blocker therapy, switching to latanoprost, when medically appropriate, may provide a further mean reduction in IOP.

Modelling
Although a formal model was not employed, the authors used assumptions about resource use and simple formulae to estimate the monthly costs of glaucoma medicines.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. In effect, a cost-consequences analysis was performed.

Direct costs
The resource quantities and the costs were not reported separately. It would appear that the health service costs were included in the analysis. Values for the direct costs included in the analysis were not reported. All costs appear to have been based on values reported in published sources (see Other Publications of Further Interest). Assumptions about the quantities of medicines consumed were used to determine values for medicine costs. Discounting was not relevant. The study reported the average costs. The price data appear to have been extracted from 2001 publications.

Statistical analysis of costs
There was no report of any statistical analyses of the quantities or costs.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
There was no report of sensitivity analyses having been carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost per person per month pre-enrolment (mean +/- SD) was $66.71 (+/- 99.80) (95% confidence interval, CI: 33.44 - 99.99) for the latanoprost monotherapy group, $53.98 (+/- 19.12) (95% CI: 49.55 - 58.51) for the latanoprost plus beta-blocker group, and $75.67 (+/- 92.45) (95% CI: 44.85 - 106.50) for the brimonidine plus beta-blocker group, (p=0.27). This cost was for beta-blocker alone prior to treatment in the assigned groups.

The cost per person per month post-enrolment (mean +/- SD) was $53.63 (+/- 11.95) (95% CI: 49.64 - 57.61) for the latanoprost monotherapy group, $83.19 (+/- 79.29) (95% CI: 64.82 - 101.56) for the latanoprost plus beta-blocker group, and $106.20 (+/- 134.59) (95% CI: 61.32 - 151.07) for the brimonidine plus beta-blocker group, (p=0.038).

The total difference in cost per person per month (mean +/- SD) from pre-enrolment to post-enrolment was -$13.08 (+/- 101.08) (95% CI: -46.79 - 20.62) for the latanoprost monotherapy group, $29.21 (+/- 81.52) (95% CI: 10.33 - 48.10) for the latanoprost plus beta-blocker group, and $30.53 (+/- 134.43) (95% CI: -14.30 - 75.35) for the
brimonidine plus beta-blocker group, (p=0.090).

The cost of adverse events was included in the costing.

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

**Authors' conclusions**
For patients uncontrolled on beta-blocker therapy, switching to latanoprost when medically appropriate may provide a further mean reduction in intraocular pressure (IOP) and save costs compared with adding latanoprost or brimonidine adjunctively.

**CRD COMMENTARY - Selection of comparators**
A justification was not given for the choice of the comparators. You should decide if they are a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on the outcomes at both the last recorded study visit and the 12-month follow-up, which was appropriate for the study question. The study sample appears to have been representative of the study population. The patient groups were shown to be comparable at analysis. The analysis of effectiveness appears to have been handled credibly.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The analysis was, in effect, a cost-consequences study.

**Validity of estimate of costs**
Full details of the costs used in the analysis were not reported. Thus it is not possible to say whether all relevant categories of cost, and all relevant costs within each category, were included in the analysis. As it was unclear whether or not any costs had been omitted, it is not possible to comment on the effect that any omissions might have had on the authors' conclusions. The costs were not reported separately from the quantities. Neither the costs nor the quantities were subjected to a sensitivity analysis. The prices appear to have been extracted from 2001 publications. Charges were not used to proxy prices.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively. The study considered a relatively small number of patients from clinics in two cities in the USA, and the authors’ conclusions do not reflect this limitation to their study. The authors reported a number of further limitations to their study. First, it had insufficient statistical power to evaluate IOP for a parallel designed trial. Second, the times when the pressures were measured throughout the day were not controlled. Third, the study design was retrospective. Finally, the study involved only a relatively short-term follow-up period (one year).

**Implications of the study**
The authors suggested that more information, on a prospective basis, is required on the costs and frequency of visits and medicine changes. They also suggested that long-term (5 years or longer) studies should be carried out effectively to evaluate visual field and optic disc changes associated with the three different medications investigated in this study.
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Other publications of related interest


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