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.

CRD summary
The objective was to assess the cost-effectiveness of three prostaglandin-based treatment sequences, for patients with primary open-angle glaucoma or ocular hypertension. The authors concluded that the economic and clinical benefits of medical management could be optimised by minimising therapy switches. The reporting and methods were good, and the authors’ conclusions seem appropriate, with the latanoprost sequence being the most cost-effective option, but the reliability of the results is unclear.

Type of economic evaluation
Cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of three prostaglandin-based treatment sequences, for patients with mild-to-moderate primary open-angle glaucoma or ocular hypertension, with no visual field loss, who were eligible for long-term topical hypotensive therapy, according to the NHS Do Once and Share, Glaucoma Clinical Care Pathway.

Interventions
The three prostaglandin-based treatment sequences allowed up to three lines of treatment. The sequences differed in their first-line prostaglandin analogue: latanoprost, bimatoprost or travoprost. The second- and third-line treatments were the addition or substitution of timolol, and then dorzolamide.

Location/setting
UK/out-patient secondary care.

Methods
Analytical approach:
A Markov model was developed to assess the costs and benefits of the three sequences, over 10 years. The authors hypothesised that cost-effectiveness could be optimised by minimising therapy switches. The model was based on three triggers for therapy change: intolerance to treatment; intraocular pressure not below target level; and progression in visual field defect. The average age of patients at baseline was assumed to be 65 years. The authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The key effectiveness inputs were the expected rates of therapy switching, for each treatment, due to the three triggers. Treatments differed in tolerance and the achievement of intraocular pressure targets. The rate of disease progression did not differ by treatment, but differed by whether the intraocular pressure targets were met. For intolerance, the rates of hyperaemia were used as a proxy, and switch rates were from a mixed-treatment comparison with 72 studies, identified by a systematic review. Switches due to non-compliance were based on expert opinion. The relative difference in intraocular pressure (after three months), for each treatment, was from a mixed-treatment comparison of 18 studies from the systematic review; the absolute on-treatment intraocular pressure over time was predicted using a meta-regression of data from 73 studies. Disease progression was from three clinical trials. The main analysis assumed a 50:50 mix of low- to high-risk patients.

Monetary benefit and utility valuations:
The utility values were applied to the four glaucoma health states. The ocular hypertension state was assumed to have the same utility as the UK population norm, as it had no symptoms. Age-specific, UK population norm utility values were from a 1999 published UK study, in which utility was measured using the EQ-5D. The other health states were based on a 2003 published study, which used visual acuity scores to predict the ocular utility values.

Measure of benefit:
The measures of benefit were the reduction in glaucoma progression, reduction in low vision, and improvement in quality-adjusted life-years (QALYs). Future QALYs were discounted at an annual rate of 3.5%.

Cost data:
The direct costs of glaucoma treatment were considered. The cost items included drug acquisition, out-patient visits, additional consultation time, surgery, and the annual cost of low vision (non-treatment and care costs). Monthly UK list prices were used to calculate the total cost of medical therapy. The frequency of out-patient visits was based on the NHS Do Once and Share treatment pathway. The cost per hour of additional consultant or nurse time was from the Personal Social Services Research Unit. The cost of extra optometrist time was from a published paper. The annual cost of low vision was from a published paper and the Personal Social Services Research Unit. All costs were reported in 2008 to 2009 prices. Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
A sensitivity analysis was conducted on the rate of switching, due to intolerance, using estimates from an expert consultant ophthalmologist. The model was run separately for low- and high-risk patients.

Results
Over 10 years, latanoprost first-line resulted in 5.87 QALYs at a total cost of £6,086.40 per patient; bimatoprost first-line resulted in 5.85 QALYs at a cost of £6,160.04 per patient; and travoprost first-line resulted in 5.85 QALYs at a cost of £6,211.70 per patient.

Latanoprost was dominant, as it was most effective and least costly. With latanoprost, patients spent on average six to seven months longer on first-line therapy, before requiring a treatment switch, and 14 to 15 months longer on medical therapy, in general, compared with the other two sequences. Latanoprost patients had a delay of 12 months to progression in glaucoma severity, compared with bimatoprost, and 13 months compared with travoprost.

Latanoprost remained dominant in the sensitivity analysis. It produced the most QALYs over 10 years for both the low- and high-risk cohorts. For the high risk cohort, it remained dominant, having the lowest overall 10-year cost per patient. For the low risk cohort, it was no longer the cheapest alternative, with bimatoprost being around £20 cheaper over 10 years, per patient.

Authors' conclusions
The authors concluded that the economic and clinical benefits of medical management could be optimised by minimising therapy switches.

CRD commentary
Interventions:
The authors stated that there was a wide range of topical medical therapies licensed for glaucoma, and their analysis was restricted to sequences starting with prostaglandin analogue. They justified this by stating that the UK National Institute for Health and Clinical Excellence (NICE) recommended such sequences. The sequences were chosen based on logic and the evidence available.

Effectiveness/benefits:
The effectiveness estimates and their sources were clearly reported. The authors used systematic methods to identify relevant studies, which should minimise selection bias. Mixed-treatment comparisons were appropriate as they synthesise all available evidence. The authors pointed out that hyperaemia as a proxy for intolerance could underestimate the treatment switch rate. Sensitivity analysis showed that the results were robust to this variation. The utility values appear to have been from appropriate populations, but their sources should be checked to assess the methods of valuation.
Costs:
The costs were appropriate for the adopted perspective. The costs and their sources were clearly reported. Appropriate national UK sources were used. The authors stated that all costs were reported in 2008 to 2009 prices, but they did not report how the costs were inflated. Future costs were appropriately discounted.

Analysis and results:
The model was clearly described, with a diagram provided. The results of the analysis were clearly reported. The latanoprost strategy was clearly dominant, in the main analysis, but a full incremental analysis of the costs and benefits of each alternative would have helped to assess the non-strictly dominated strategies. The authors completed a limited analysis of uncertainty. Only one parameter was varied and only one alternative value was assessed. A probabilistic analysis, in which the overall parameter uncertainty is assessed, could have been conducted. Given the lack of a full sensitivity analysis, the reliability of the results is unclear. The authors did not justify the limited scope of their sensitivity analysis.

Concluding remarks:
The reporting and methods were good, and the authors’ conclusions seem appropriate, but the reliability of the results is unclear.

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