The long-term outcomes of four alternative treatment strategies for primary open-angle glaucoma
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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.

CRD summary
The study evaluated the long-term health and cost-effectiveness of various strategies for the treatment of primary open-angle glaucoma. The authors concluded that aiming for a low intraocular pressure in all glaucoma patients was optimal and that initial treatment with latanoprost was also an acceptable cost-effective strategy. The validity of the data estimates in the model was unclear, but the methods and results were fully transparent. The authors’ conclusions appear to be a reasonable assessment of the findings.

Type of economic evaluation
Cost-utility analysis

Study objective
The study evaluated the long-term health and cost-effectiveness outcomes of four alternative pharmacotherapy strategies for primary open-angle glaucoma compared with usual care and no care in a hypothetical population of first-time ophthalmologist visitors (mean age 68 years).

Interventions
The strategies evaluated were: usual care including timolol first-line medication, an initial target pressure of 21 mmHg and 12 month eye tests; no care including only the initial ophthalmologist visit; latanoprost first-line medication, an initial target pressure of 21mmHg and 12 month eye tests; initial timolol first-line medication, targeted initial pressure of 15mmHg and 12 month eye tests; timolol first-line, an initial target pressure of 21mmHg and six month eye tests; and timolol first-line medication, an initial target pressure of 21mmHg and 24 month eye tests. Medication switching occurred when side-effects were reported at follow-up visits and included the choice of timolol, latanoprost, dorzolamide (carbonic anhydrase inhibitor) and brimonidine (alpha-adrenergic agonist).

Location/setting
The Netherlands/secondary care.

Methods
Analytical approach:
A discrete event simulation was used to simulate the lifetime health and resource use of the individual patients. The development and validation of the model was previously published (van Gestel 2010a, see Other Publications of Related Interest). The authors stated that the study took a societal perspective. The time horizon was 15.4 years (the average duration of simulated lives). The model included 3,000 patient simulations.

Effectiveness data:
The population characteristics were based on study populations in the Early Manifest Glaucoma Study and the Collaborative Initial Glaucoma Treatment Study. The treatment effectiveness parameters were derived from a number of clinical trials (details were provided in a supplementary online appendix). The relative risk of formation of cataracts was incorporated. Data from administrative databases and published studies were used to build the relationships and networks between the events and subsequent treatments. The course of glaucoma was assumed to be represented by patients with two symmetrically affected eyes. Look-up tables and parameter distributions were assigned to allow random selection of attributes for each individual being evaluated in the model.
Monetary benefit and utility valuations:
Utilities were based on the authors previous estimates from observational research of patient quality of life with ocular hypertension and primary open-angle glaucoma (van Gestel 2010b, see Other Publications of Related Interest) and estimates using the Health Utilities Index (mark 3).

Measure of benefit:
The measure of benefit used was quality-adjusted life years (QALYS) discounted at 1.5% per year.

Cost data:
Direct medical costs included ophthalmologist visits, visual field tests, medications, surgery, home care, low-vision rehabilitation and aids, and nursing home costs. Non-medical costs assessed were transport costs, productivity costs and informal care costs. Unit costs were provided and used in the simulation modelling. The cost values were presented in 2006 Euros (EUR) and discounted at 4.0% per year.

Analysis of uncertainty:
Sensitivity analyses were performed on specific scenarios which included modelling the worse eye only, a non-linear relationship between visual field loss, and quality of life and other assumptions of the model estimates. Probabilistic sensitivity analyses were also undertaken. Graphs of the results were presented.

Results
Over a 15.4-year period, the usual care strategy had discounted mean costs of EUR 23,892 and discounted QALYs of 10.37. The no care strategy (except initial visit) had discounted mean costs of EUR 42,099 and discounted QALYs of 9.19. The latanoprost strategy had discounted mean costs of EUR 23,982 and discounted QALYs of 10.38. The timolol strategy with 12 month eye tests had discounted mean costs of EUR 22,343 and discounted QALYs of 10.49. The timolol strategy with six month eye tests had discounted mean costs of EUR 23,753 and discounted QALYs of 10.38. The timolol strategy with 24 month eye tests had discounted mean costs of EURO 23,573 and discounted QALYs of 10.36.

Incremental ratios for each strategy compared with the usual care strategy were presented. For the latanoprost strategy compared with usual care, the incremental cost per QALY was EUR 12,931. The timolol strategy with 12 month eye tests dominated usual care (it was more effective and less costly). For the timolol strategy six month eye tests compared with usual care, the incremental cost per QALY was EUR 173,486. For the timolol strategy with 24 month eye tests compared with usual care, the incremental cost per QALY was EUR 21,516. The no care strategy was dominated by usual care.

The authors reported that in the sensitivity analyses, the results were most influenced by the costs of eye care, the utility loss of progression, and the effect of intraocular pressure reduction. The probabilistic sensitivity analyses indicated that the strategy initial latanoprost treatment would have a probability of 60% of being cost effective at a threshold of EUR 40,000 per euro per QALY or 50% at EUR 14,000.

Authors' conclusions
The authors concluded that aiming for a low intraocular pressure in all glaucoma patients was optimal and that initial treatment with latanoprost with a target pressure of 21mmHg and 12 month eye tests was also an acceptable cost-effective strategy.

CRD commentary
Interventions:
The strategies were sufficiently described in the report and appeared to represent a number of alternative combinations of potential strategies. The generalisability or clinical relevance of the strategies outside of the authors' setting was not discussed. Although the authors highlighted that if early surgical intervention was not an option, then a reanalysis of the model may be warranted.

Effectiveness/benefits:
The risks associated with macular degeneration, disease progression, complications, health-related quality-of-life and all of their associated interactions and influences were based on published studies and relevant data sources. The
complexity of the modelling and the associated parameter distributions were presented in the paper and in supplementary online files. Whilst there was not extensive reporting surrounding the identification and selection of the initial baseline data, full details of the methods used to characterise and use the data were provided. It was not explicitly discussed, but it would appear relevant clinical sources have been used.

Costs:
The unit costs were presented in a separate online appendix to the paper and were based on nationally representative Dutch sources. The scope of the costs involved in the study was comprehensive and covered a societal perspective. The appendix provided a break-down of the health system costs.

Analysis and results:
The authors referenced a paper that addressed the structural and face-validity of their simulation model. The modelling was complex and a reasonable level of detail was presented in the paper. The authors highlighted some limitations of their study, including the absence of testing for visual field testing accuracy and the applicability of their findings to different jurisdictions with varying clinical practices and prices. The analyses were comprehensive and sensitivity results clearly presented.

Concluding remarks:
The validity of the data estimates used in the model was somewhat unclear, but the methods and results were fully transparent. The conclusions reached by the authors appear to be a reasonable assessment of the study findings.

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