Costs and persistence of carbonic anhydrase inhibitor versus alpha-2 agonists, associated with beta-blockers, in glaucoma and ocular hypertension: an analysis of the UK-GPRD database
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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
This study compared the clinical and economic impact of alpha-2 adrenergic agonists and carbonic anhydrase inhibitors (CAIs), in combination with a beta-blocker, for the treatment of glaucoma. Using a national database, the authors concluded that CAIs plus beta-blockers were more persistent than, and as expensive as, alpha-2 agonists plus beta-blockers. The study appears to have been satisfactorily carried out, although there were some methodological limitations associated with the clinical data source. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study compared the clinical and economic impact of two glaucoma treatments, which were alpha-2 adrenergic agonists and carbonic anhydrase inhibitors (CAIs), both of which were given in combination with a beta-blocker.

Interventions
The two glaucoma therapies were alpha-2 agonists (brimonidine) and CAIs (brinzolamide or dorzolamide) and the beta-blockers were betaxolol, levobunolol, metipranolol, timolol, or cartelol.

Location/setting
UK/secondary care.

Methods
Analytical approach:
This economic evaluation was based on data from a single study, with a follow-up of four years. The authors stated that the perspective of the National Health Service (NHS) was adopted.

Effectiveness data:
The clinical data came from a retrospective cohort study, namely the United Kingdom General Practitioner Research Database (UK-GPRD), which collected medical information from a representative sample of general practitioner (GP)s. There were 1,164 patients in the alpha-2 agonist group and 5,581 patients in the CAI group. Considerable data management was performed to convert the events reported in the database into data relevant for this analysis. Patients with at least 100 days of follow-up were included and the total length of follow-up was four years. Regression analysis was performed to take into account the different durations of follow-up for the two groups. The key clinical endpoint was treatment failure. Time to failure, another relevant outcome, was adjusted for age, gender, co-morbidities and the duration of follow-up.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
No summary benefit measure was used. The primary clinical endpoint was treatment failure, which was defined as prescription change. This included the replacement or discontinuation of any drug initiated for glaucoma, the addition
of any medication to the current treatment, and surgery or laser therapy.

Cost data:
The economic analysis included the costs for glaucoma care of: surgical and laser treatments; hospitalisations; medications; and medical visits to GPs or specialists, including prescription renewals by telephone. The resource use data were derived from the UK-GPRD, with some assumptions made for the duration of visits. The drug costs came from the British National Formulary. Other costs came from official NHS sources and a published study. The price year was 2005 and all costs were in UK pounds sterling (£).

Analysis of uncertainty:
Not investigated.

Results
The adjusted treatment failure after one year was 64.3% with alpha-2 agonists and 57% with CAIs. This difference was statistically significant (p<0.001) and was maintained over the subsequent three years.

The unadjusted hazard ratio for failure was less with CAIs than with alpha-2 agonists (odds ratio, OR: 0.83, 95% confidence interval, CI: 0.76 to 0.89, p<0.0001) and remained statistically significant after adjustment (OR: 0.82, 95% CI: 0.75 to 0.88, p<0.0001).

The average time to 50% failure was 7.2 months with alpha-2 agonists and 9.2 months with CAIs and this difference was statistically significant.

Total costs were not significantly different between the two groups, with average monthly costs of £28.45 for alpha-2 agonists and £28.79 for CAIs (p=0.81). Adjusting these costs for follow-up duration, did not alter this conclusion, with annual total costs of £356.80 for alpha-2 antagonists and £348.04 for CAIs (p=0.61).

Authors' conclusions
The authors concluded that, from the perspective of the UK NHS, glaucoma therapy with CAIs plus beta-blockers was more persistent than, and as expensive as, treatment with alpha-2 agonists plus beta-blockers.

CRD commentary
Interventions:
The selection of the comparators was appropriate given that two commonly used classes of drugs were selected. However, the authors noted that new drugs were approved during the study period, and these might have impacted on the decisions to change treatments.

Effectiveness/benefits:
The clinical evidence came from the retrospective analysis of an administrative database. The authors noted some limitations of their analysis, mainly related to this use of administrative data, which did not allow a comprehensive analysis of the efficacy of treatments. For example, the reasons for modifying treatments were not documented, but the authors assumed that these changes were made due to intolerance or lack of efficacy. Furthermore, the retrospective analysis precluded any verification of data accuracy. However, the internal validity was enhanced by the large sample size and significant differences between groups were detected. The two groups were also comparable at baseline with respect to their demographic and clinical characteristics except for the time since diagnosis and mean duration of follow-up, which were both significantly longer for the alpha-2 agonist group. The potential impact of these baseline differences was assessed and appropriate statistical adjustments were made. The follow-up appears to have been long enough to capture the impact of the two therapies and extensive data management was performed to adapt the administrative data for this analysis. The UK-GPRD contained real-life estimations, which could be more relevant to clinicians than data from randomised controlled trials. In general, the authors tried to minimise the impact of methodological limitations. They pointed out that the main clinical endpoints were ones commonly used in the analysis of claim data.

Costs:
The categories of costs and the sources of the unit costs were consistent with the perspective and a breakdown of cost items was provided. Data on the resource consumption were reported for most items, but the unit costs were not. It was not clear whether any discounting was carried out, although it was relevant given the four-year time horizon. Standard statistical analyses of the costs were appropriately performed to investigate the statistical significance of cost differences.

Analysis and results:
A synthesis of the costs and benefits was not relevant given the cost-consequences framework. The findings were clearly presented and discussed. The issue of uncertainty was not investigated. Some potential limitations related to the design of the study were pointed out.

Concluding remarks:
On the whole, the study appears to have been satisfactorily carried out, although there were some methodological limitations associated with the clinical data source. The authors’ conclusions appear to be valid.

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