Cost-effective analysis by Markov Chains of open-angle glaucoma therapy: preliminary results

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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
First line pharmacological treatment with a beta-blocker for primary open-angle glaucoma (POAG). Four different drugs were compared: timolol, betaxolol, carteolol and levobunolol. Doses/regimens of the drugs were not described. At the start of the observation period, every patient received a complete eye test and a series of specialised examinations (tonometry, campimetric, provocative test). During the remainder of the period, these examinations were uniformly distributed according to the efficacy of therapy. Following initial pharmacotherapy, patients may require second level pharmacotherapy, parasurgery, or surgery.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Few details were provided, but the study population appeared to comprise patients attending a named ophthalmology out-patient department because of glaucoma.

Setting
The setting was secondary care, namely an ophthalmology out-patient department of the University of Turin in Italy.

Dates to which data relate
Dates for the analysis of effectiveness and resource use were not provided. The price year was 1998-1999.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
It is unclear whether the costs were derived from the same patients used for the effectiveness analysis.

Study sample
Seventy patients were recruited (33 males and 37 females), with an overall mean age of 61 years (standard deviation 13 years). No details were provided concerning sample size calculation or estimation of statistical power, method of patient selection, numbers of patients receiving each drug, number of patients who refused to participate, or number of patients excluded from the sample. Due to lack of detailed information in the paper, it was not possible to judge whether the
group recruited was appropriate for the clinical study question.

**Study design**
The study took the form of a single-centre case series with one-year follow-up. The loss to follow-up was not reported.

**Analysis of effectiveness**
The authors stated that they used 'equivalent months of useful therapy' as a measure of efficacy, and described the following grading system for the usefulness of pharmacological therapy:

1 = monotherapy was sufficient to control IOP;
0.5 = second drug required;
0.3 = third drug required.

The data were analysed retrospectively. The baseline comparability of groups receiving the different drugs was not reported. It is not clear whether all the patients in the case series were accounted for in the analysis (thus making it difficult to judge whether the analysis was based on intention to treat or treatment completers only).

**Effectiveness results**
The mean equivalent months of useful therapy per patient for the four different beta-blockers were as follows: levobunolol 10.8; carteolol 10.3; timolol 9.6; and betaxolol 7.4.

**Clinical conclusions**
From the information provided, it appears that levobunolol was the most effective strategy, followed by carteolol, then timolol, and betaxolol appeared to be the least effective.

**Modelling**
A Markov model was used to compare the cost-effectiveness of four different beta-blockers (timolol, betaxolol, carteolol and levobunolol) in the treatment of POAG. The data for each patient related to a collection period of one year while the Markov analysis was carried out with transitional probabilities at fixed intervals of one month.

**Measure of benefits used in the economic analysis**
The mean equivalent months of useful therapy per patient for the four different beta-blockers was reported (see effectiveness results above), with associated marginal values.

**Direct costs**
The costs considered were those of the Italian national health service. The authors stated the following:

the monthly costs of the treatments were estimated by summing the cost of buying the drug with that of treating adverse reactions, wastage of material and failures due to poor compliance;

the different alternatives and the costs of the other health resources consumed (e.g. medical examinations) were estimated;

for surgery, costs to the health system were deduced from the national rates for hospital patients.

Costs were shown graphically per month for clinic visits, measurement of IOP, assessment of visual field and drug prescription. Costs and quantities were not reported separately. The cost data may have been derived from two papers.
cited at the end of the article, however, since the article was not formatted in terms of linking cited references to reported data, it is not possible to be certain where the cost estimates were derived from. Discounting was not mentioned, but the authors stated that the data for each patient referred to a collection period of one year and this period was not extended in the model. Marginal costs were reported. The price year used was 1998-1999.

**Statistical analysis of costs**
Costs per individual treatment strategy were reported as mean point estimates.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
Italian lira (L).

**Sensitivity analysis**
Not reported.

**Estimated benefits used in the economic analysis**
The mean equivalent months of useful therapy per patient for the four different beta-blockers were as follows: levobunolol 10.8; carteolol 10.3; timolol 9.6; and betaxolol 7.4.

The marginal values were as follows: carteolol versus timolol -0.7; levobunolol versus timolol 1.2; levobunolol versus betaxolol 3.4; and carteolol versus levobunolol 0.5.

**Cost results**
The mean direct health costs per patient per month of therapy were highest in the first month, diminishing from the start of the second month and then levelling out through the remainder of the observation period. However, the pharmaceutical expense remained constant throughout the year (24% of annual health costs).

The mean annual treatment costs per patient with POAG were as follows: carteolol L312,435; timolol L322,545; levobunolol L627,348; and betaxolol L793,746.

The following marginal costs were reported: carteolol versus timolol L10,110; timolol versus levobunolol L304,803; levobunolol versus betaxolol L166,398; carteolol versus levobunolol L314,913.

**Synthesis of costs and benefits**
The cost-effectiveness ratios for the four drugs were as follows: carteolol L30,188; timolol L33,624; levobunolol L58,099; and betaxolol L106,878.

The analysis of marginal cost-effectiveness revealed the following: timolol was dominated with respect to carteolol; betaxolol was dominated with respect to levobunolol; levobunolol had a marginal cost-effectiveness of L252,901 relative to timolol; and levobunolol had a marginal cost-effectiveness of L702,089 relative to carteolol.

**Authors’ conclusions**
The most cost-effective strategy was that using carteolol as the drug of first choice. Timolol and betaxolol were dominated by carteolol and levobunolol respectively.
CRD COMMENTARY - Selection of comparators
The authors explained that the selected four drugs were used frequently in their own clinic. However, there was no
description of the differences between the drugs, e.g., whether one or more may have been used for more severe cases
of glaucoma, or why it was important to know about their relative clinical effectiveness and cost-effectiveness. In
addition, the generalisability of the findings was unclear, as a discussion was not included; the paper was published as a
brief report only.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study, involving retrospective analysis of a case series. Case series
may be prone to selection bias and the data available for retrospective analysis may be of limited quality. It was difficult
to ascertain to what degree the study sample was representative of the study population as few details of the study
groups were provided. In addition, it was unclear whether the study groups were comparable since baseline data were
not reported. Methods used for data analysis were not described. The authors derived a measure of health benefit that
they termed 'the mean equivalent months of useful therapy per patient for each drug'. However, they did not describe
how this measurement was calculated, nor did they define what 'useful therapy' meant.

Validity of estimate of measure of benefit
See comments under Validity of estimate of measure of effectiveness.

Validity of estimate of costs
All categories of cost relevant to the perspective adopted (national health service) were included in the analysis. Since a
detailed breakdown of all costs was not provided, it was not possible to determine whether all relevant costs were
included in the analysis. Costs and quantities were not reported separately. Data relating to resource use and prices
appeared to have been taken from published papers. However, since references were not linked to the text, it was not
possible to identify sources of data with certainty. Sensitivity analyses of quantities and prices were not conducted. This
may limit the interpretation of the study findings.

Other issues
This paper was published as a brief report; consequently many details were lacking. The authors did not compare their
results with other comparable studies, the issue of generalisability to other settings was not addressed, and limitations of
the study were not discussed. The authors did not appear to present their results selectively and their conclusions
appeared to reflect the scope of the analysis. A more detailed report of the study would be welcome, and it is possible
that this is forthcoming since the title of the paper suggests that these findings are preliminary.

Implications of the study
The authors state that it is important to have access to reliable data about clinical and economic outcomes of treatment
for POAG in order to plan the best cost-effective therapeutic strategies for the health service, and for society, and it
would therefore be desirable to set up data banks where the necessary information could be obtained.

Source of funding
None stated.

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