An economic assessment of inhaled formoterol dry powder versus ipratropium bromide pressurized metered dose inhaler in the treatment of chronic obstructive pulmonary disease

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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 health technologies considered were three treatment strategies for chronic obstructive pulmonary disease (COPD): inhaled formoterol dry powder 12 microg twice a day, inhaled formoterol dry powder 24 microg twice a day and ipratropium bromide 4 microg four times a day in a pressurised metered dose inhaler.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with COPD. Specific inclusion/exclusion criteria were not reported.

Setting
The setting was not clearly stated but it is likely to have been primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The clinical effectiveness and resource use data evidence were taken from a previously published study; Dahl et al 2001 (see ‘Other Publications of Related Interest’ below for bibliographic details). The price year was 2002.

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

Study sample
The study comprised 780 patients, but the number allocated to each treatment was not reported. No power calculations were reported in the paper. The method of sample selection was not stated.

Study design
The study was a multi-centre randomised controlled trial. Patients were followed up for 12 weeks. The paper did not report the extent of loss to follow-up. It was reported that the trial was double blind.

Analysis of effectiveness
The trial data were analysed on an intention to treat basis. The primary health outcomes assessed by the trial were normalised forced expiratory lung function in one second (FEV1) and improvement in quality of life (QOL) as measured by the St George's Respiratory Questionnaire (SGRQ).

FEV1 values, expressed in litres/second, were measured as follows:

baseline FEV1 plus the difference of treatment group contrasts relative to placebo of normalised area under the curve-FEV1 following the morning dose of study medications on the last day of treatment (12 weeks);

formoterol arms were further reduced by 0.04 and 0.02 litres, respectively (the amount by which the FEV1 measures for these arms exceeded the baseline FEV1 measures for placebo and ipratropium bromide).

Differences in QOL scores were measured between baseline and end-of-study SGRQ total scores. The baseline value for the ipratropium bromide arm was further adjusted by the amount it exceeded the other arms: 1.6 points.

Other efficacy variables were assessed in the trial but were not fully reported in this paper.

No details of the baseline characteristics of the patients included in the trial were reported, and no comment was made as to whether the groups were comparable.

**Effectiveness results**

The following FEV1 measurements were recorded in the treatment groups:

- placebo = 1.290 l/s;
- ipratropium bromide 40microg = 1.427 l/s;
- formoterol 12microg = 1.513 l/s; and
- formoterol 24microg = 1.484 l/s.

The improvements in quality of life were recorded in the treatment groups:

- placebo = 1.5;
- ipratropium bromide 40microg =1.1;
- formoterol 12microg = 6.6; and
- formoterol 24microg = 4.8.

**Clinical conclusions**

The authors concluded that formoterol 12 microg was the most clinically effective treatment of the four options considered in this study.

**Modelling**

A model was used to estimate the costs associated with each treatment.

**Measure of benefits used in the economic analysis**

The measures of health benefit used in the economic analysis were FEV1 and change in quality of life. Quality of life was assessed using the St George’s Respiratory Questionnaire. This information was taken from the clinical study.
Direct costs
It appears that the direct costs of the healthcare payer were assessed in this analysis. The costs of the trial drugs and rescue medications (salbutamol) were included in the assessment of costs. The costs of the steroids, physician visits and other COPD related healthcare costs were the same in all treatment groups. These costs were therefore excluded from the analysis. Quantities of these drugs consumed were taken from the clinical trial and their unit cost was taken from average wholesale prices in the Red Book. Unit costs and quantities consumed were reported in the paper. The price year appears to have been 2002. Costs were not discounted, as they were incurred over a period of 12 weeks.

Statistical analysis of costs
No statistical analysis of costs was undertaken.

Indirect Costs
No indirect costs were included in the study.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was undertaken to assess variability in the data. Sensitivity analysis on FEV1 was conducted using the lower and upper 95% confidence intervals (CIs) of changes as reported in the reference clinical trial. For the other variables, the ranges were plus and minus 50% of baseline value.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results reported above.

Cost results
The following total costs were identified for each treatment group:

- placebo = $38.93;
- ipratropium bromide 40microg = $76.34;
- formoterol 12microg = $214.91; and
- formoterol 24microg = $418.92.

Synthesis of costs and benefits
The average costs per FEV1 were identified for each treatment group:

- placebo = $30.18;
- ipratropium bromide 40microg = $53.50;
- formoterol 12microg = $142.04; and
- formoterol 24microg = $282.29.

The average costs per change in QOL score were identified for each treatment group:
placebo = $25.96;

ipratropium bromide 40microg = $69.40;
formoterol 12microg = $32.56; and
formoterol 24microg = $87.28.

An incremental cost-effectiveness analysis was undertaken. This showed that the incremental cost-effectiveness ratio of formoterol 12 microg over a placebo was $34.51 per QOL score change. Both the ipratropium bromide 40 microg and formoterol 24 microg were dominated when considering the change in QOL. The incremental cost-effectiveness in terms of FEV1 for ipratropium bromide 40 microg versus placebo was $273.03 per FEV1. The incremental cost-effectiveness ratio of formoterol 12 microg versus ipratropium bromide 40 microg was $1,611.32 per FEV1. Formoterol 24 microg was a dominated treatment in terms of FEV1.

Sensitivity analysis indicated that varying the baseline data in the study did not alter the overall results of the economic analysis.

Authors’ conclusions
The authors concluded that the formoterol 12 microg twice a day is the most clinically and cost-effective of the treatments considered.

CRD COMMENTARY - Selection of comparators
The choice of the comparator, namely ipratropium bromide, was justified as it represented a widely used agent in the management of COPD. In addition, the three treatment options considered in this study were appropriately compared to placebo. You should consider how the options relate to current practice in your setting prior to applying the results of this study.

Validity of estimate of measure of effectiveness
The clinical effectiveness data used in this analysis was taken from a randomised, double-blind, controlled trial. This was an appropriate study design. Power calculations were not reported and no statistical analysis was carried out. No details of the baseline characteristics of the trial sample were included in the paper. This means that it is not possible to comment on whether the patient sample was representative of the patient population, or whether the treatment groups were comparable at baseline, hence confounding factors may be high and may bias the effectiveness results. Little information on the analysis of the clinical data was included in the paper.

Validity of estimate of measure of benefit
The measure of benefit was derived directly from the clinical study.

Validity of estimate of costs
The perspective of the study was not explicitly stated, but was consistent with that of the healthcare payer. In the clinical study the use of steroids, physician visits and other related health care consumption were the same in all four treatment groups, and were therefore not included in the analysis. In addition, long term consequences of therapy were not included in the cost analysis. However, the authors showed that taking account of hospitalisations may have changed the cost-effectiveness ratios. They suggested that additional research on long-term consequences of therapy would be more informative. The paper provided a breakdown of the resource use and unit costs. This assists the scope of generalising the study to other settings. A price year was identified in the paper. This fact also adds to the generalisability of the study and will allow future reflation exercises. No statistical analysis of resource use was performed but a sensitivity analysis that examined the impact of changes in unit costs, resource use and clinical effectiveness was performed. This adds to the robustness of the results and the generalisability of the study findings.
Discounting was appropriately not undertaken, as costs were incurred over a period of less than two years.

**Other issues**
The authors presented their results in a comprehensive manner and their conclusions reflected their analysis. They did not directly consider how their results could be generalised to other settings. The authors did not compare their findings with those of other studies. They acknowledged the fact that the economic data were not collected prospectively alongside the clinical effectiveness data. It was also noted that patients participating in a trial may be influenced by the fact that they are in a study and therefore if the results of the study were used to alter practice, the impact might be slightly different.

**Implications of the study**
The authors did not make any direct recommendations for further research or changes to practice.

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**Bibliographic details**

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**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

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