Cost-effectiveness of long-acting bronchodilators for chronic obstructive pulmonary disease

Oba Y

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 author compared a number of long-acting bronchodilators for chronic obstructive pulmonary disease (COPD), including salmeterol, tiotropium and ipratropium. The use of bronchodilators was also compared with placebo.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with moderate to severe COPD.

Setting
The setting was secondary care. The economic study was undertaken in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1980 and 2006. The price year was 2005.

Source of effectiveness data
The clinical and epidemiological data used in the economic evaluation were St. George's Respiratory Questionnaire (SGRQ) scores, hospitalisation rates and unscheduled physician visits.

Sources searched to identify primary studies
The clinical effectiveness data were derived from a number of randomised controlled trials.

Methods used to judge relevance and validity, and for extracting data
The author reported that a systematic review of the literature was conducted for the main effectiveness estimate. The literature search was conducted in MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews, and the bibliographies of published articles were examined. The search was limited to English language studies of patients aged older than 40 years, which were randomised and placebo-controlled and had blinded ascertainment of end points, at least 16 weeks’ follow-up with at least 80% follow-up data, and baseline characteristics that were well balanced or adjusted for prognostic factors.

Measure of benefits used in the economic analysis
The measure of benefits used was the QALYs gained. QALYs were calculated on the basis of the improvement by converting SGRQ scores into EuroQol-5D (EQ-5D) index scores, based on the results of a published mapping exercise (Stahl et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). Since the QALYs were gained over 1 year, discounting was not relevant and was not performed.

**Direct costs**
The direct costs to the third-party payer were included in the analysis. These included the costs of medication, unscheduled physician and emergency department visits, and hospitalisation. The resource use data were derived from studies included in the effectiveness review and the author's own assumptions. The author assumed that 10% of unscheduled visits occurred in emergency departments, that a 7-day course of prednisone was used for outpatient treatment of COPD exacerbations, and that the average length of stay in hospital was 4.9 days. The costs of medications were determined on the basis of the average wholesale price. Average costs of hospitalisations were derived from Medicare reimbursements, which were converted into costs using cost-to-charge ratios. The cost of a physician visit was based on average reimbursements of the Current Procedural Terminology. Other costs were derived from published studies. Since the costs were incurred during 1 year, discounting was not relevant and was not performed. The costs were adjusted to 2005 prices using the Consumer Price Index (CPI). The study reported the incremental costs.

**Statistical analysis of costs**
The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**
Productivity costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were performed using the 95% confidence intervals of the costs of hospitalisations, unscheduled visits and incremental QALYs; the Federal Supply Schedule cost of bronchodilators was also used. Furthermore, in order to examine the uncertainty in mean costs and effects, cost-effectiveness acceptability curves were produced.

**Estimated benefits used in the economic analysis**
Compared with placebo, treatment with tiotropium resulted in a net gain of between 0.032 and 0.045 QALYs.

Compared with placebo, treatment with salmeterol resulted in a net gain of between 0.026 and 0.030 QALYs.

Compared with ipratropium, treatment with tiotropium resulted in a net gain of 0.036 QALYs.

**Cost results**
Compared with placebo, treatment with tiotropium generated additional costs of between $835 and $900 per patient.

Compared with placebo, treatment with salmeterol generated additional costs of between $1,066 and $1,119.

Compared with ipratropium, treatment with tiotropium generated savings of $391 per patient.

**Synthesis of costs and benefits**
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained).
Compared with placebo, the additional cost per QALY gained of treating patients with tiotropium ranged from $20,000 to $26,094.

Compared with placebo, the additional cost per QALY gained of treating patients with salmeterol ranged from $37,300 to $41,000.

Treatment with tiotropium was found to be dominant over ipratropium, as it was both more effective and less costly.

The results of the sensitivity analysis showed that, at a willingness-to-pay threshold of $50,000 per QALY gained, the probability that tiotropium and salmeterol were cost-effective was 93% and 67%, respectively.

Authors' conclusions
Tiotropium would appear to be more cost-effective than the alternatives and may be the preferred agent for maintenance therapy in patients with moderate to severe chronic obstructive pulmonary disease (COPD).

CRD COMMENTARY - Selection of comparators
A justification was given for using placebo as the comparator: the cost-effectiveness of long-acting bronchodilators had not been formally studied in the USA. You should decide if the comparator used represents current practice in your own settings.

Validity of estimate of measure of effectiveness
The effectiveness parameters were derived from published research based on randomised controlled trials. The author reported that the results of different studies were combined using meta-analysis. The search methods performed in the review of the literature review were reported in detail, including the sources searched and inclusion and exclusion criteria. Only randomised, placebo-controlled trials with blinding and low loss to follow-up were included in the analysis. Consequently, the studies included in the review will have had high internal validity.

Validity of estimate of measure of benefit
The measure of health benefit (QALYs) was derived from the studies included in the effectiveness review. In order to derive QALYs, the author obtained SGRQ data from the studies included in the review and applied a published formula to convert these scores into EQ-5D data. The author reported that the literature had shown a significant, strong correlation ($r > 0.6$), between SGRQ and EQ-5D scores. Since the QALYs were generated over 1 year, discounting was appropriately not performed.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the third-party payer. Given this perspective, it appears that all the relevant cost categories and costs have been included in the analysis. The resource use data were derived from published studies included in the effectiveness review, supplemented by the author's own assumptions. The unit costs were derived from published sources and, when applicable, charges were converted into costs using cost-to-charge ratios, as charges may not reflect the true cost of an intervention. Since the costs were incurred during 1 year, discounting was not relevant and was therefore not performed. The costs were converted to 2005 using the CPI. However, the use of the health care component of the CPI would have been more appropriate, as health care inflation is generally higher than overall inflation. The author evaluated uncertainty in the cost data jointly with the effectiveness data by means of a cost-effectiveness acceptability curve.

Other issues
The author reported that this analysis was the first to show the incremental costs of long-acting bronchodilators per QALY gained in patients with COPD. The issue of generalisability to other settings was addressed in the sensitivity analysis. The author does not appear to have presented his results selectively and the conclusions reflected the scope of the analysis.

The author acknowledged a number of further limitations to the study. First, indirect costs were not included as the study was performed from a third-party payer perspective. Second, comparisons between drugs were carried out using
different studies, which could have resulted in differences between the populations studied, although the author reported that the populations studied in the different studies were comparable. Third, formoterol was not evaluated because of the paucity of data. Finally, the costs of potential adverse events were not included because they are considered to be rare and to incur minimal costs.

Implications of the study
The author reports that because of wide ranges of cost-effectiveness ratios for tiotropium and salmeterol and the significant overlap between them, a large prospective head-to-head trial would help address the uncertainty and confirm the results of this analysis.

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None stated.

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Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Albuterol / analogs & derivatives / economics / therapeutic use; Bronchodilator Agents / economics / therapeutic use; Cost Savings; Cost-Benefit Analysis; Female; Hospitalization / economics; Humans; Ipratropium / economics / therapeutic use; Male; Middle Aged; Pulmonary Disease, Chronic Obstructive / drug therapy / economics; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Salmeterol Xinafoate; Scopolamine Derivatives / economics / therapeutic use; Tiotropium Bromide

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