Economic analyses comparing tiotropium with ipratropium or salmeterol in UK patients with COPD
Gani R, Griffin J, Kelly S, Rutten-van Molken M

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 cost-effectiveness of tiotropium, ipratropium, and salmeterol, for the treatment of chronic obstructive pulmonary disease. The authors concluded that tiotropium was a cost-effective alternative to ipratropium and salmeterol, and switching patients from ipratropium and salmeterol to tiotropium led to considerable cost savings for primary care trusts. The methods were valid and the extensive analysis of uncertainty enhances the validity of the authors' conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study compared the cost-effectiveness of tiotropium, ipratropium, and salmeterol, for the treatment of chronic obstructive pulmonary disease (COPD). A budget impact analysis was also performed.

Interventions
The interventions were a short-acting anticholinergic, ipratropium; a long-acting β2 agonist, salmeterol; and a long-acting anticholinergic, tiotropium. Each treatment was given with the usual care, which included short-acting β2 agonists, but excluded anticholinergic drugs and long-acting β2 agonists, except the salmeterol intervention. Salmeterol was given at a dosage of 50mg twice daily, ipratropium at 40mg four times per day, and tiotropium at 18mg once daily.

Location/setting
UK (England analysed separately from Scotland, Wales, and Northern Ireland)/primary and secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model that represented patients with mild, moderate, or severe COPD (Oostenbrink, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon was one year and the authors stated that the perspective of the UK National Health Service (NHS) was taken.

Effectiveness data:
The clinical data came from a selection of relevant studies, including six multi-centre, randomised, double-blind, double-dummy, parallel-group trials. All these trials included tiotropium and it was compared with salmeterol in three trials, ipratropium in two trials, and placebo in one trial. Additional data were from other published sources. The key input was the treatment efficacy in reducing the risk of exacerbations.

Monetary benefit and utility valuations:
The utility values were from a published study that estimated them using the European Quality of life (EQ-5D) questionnaire, with a sample of 1,235 patients from 13 countries.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of drugs, treatment of exacerbations, and COPD maintenance. The resource use data were mainly from a Delphi panel of eight clinicians and four secondary care consultants. The costs were based on UK reference prices. The costs of exacerbations were different for England compared with Scotland, Wales, and Northern Ireland. In England they were based on Health Resource Group data from a hospital database, while the Delphi panel was used for Scotland, Wales, and Northern Ireland. Costs were in UK pounds sterling (£) and the price year was 2009.

Analysis of uncertainty:
A multivariate probabilistic sensitivity analysis was undertaken to determine the uncertainty around the incremental cost-utility ratios, using pre-determined probability distributions. An additional one-way sensitivity analysis was carried out to examine the cost-effectiveness of tiotropium versus salmeterol or ipratropium in cohorts composed entirely of mild, moderate, or severe patients.

Results
In England, the total costs were £1,439 with tiotropium, £1,565 with salmeterol, and £1,631 with ipratropium. The QALYs were 0.744 with tiotropium, 0.730 with salmeterol, and 0.723 with ipratropium. In Scotland, Wales, and Northern Ireland, the total costs were £1,305 with tiotropium, £1,404 with salmeterol, and £1,427 with ipratropium. The QALYs were 0.744 with tiotropium, 0.730 with salmeterol, and 0.723 with ipratropium.

Tiotropium was the dominant strategy, as it was more effective and less expensive than the other treatments. Salmeterol dominated ipratropium.

At a threshold of £20,000 per QALY, compared with salmeterol, the probability of tiotropium being cost-effective was 97% in both England and Scotland, Wales, and Northern Ireland. Compared with ipratropium it was 99% in England and 98% in Scotland, Wales, and Northern Ireland. In all deterministic analyses, tiotropium was dominant, except in the severe group for tiotropium versus ipratropium, where the incremental cost per QALY gained was £1,600 in England and £3,450 in Scotland, Wales, and Northern Ireland.

The budget impact analysis showed that for a typical primary care trust, switching to tiotropium resulted in annual cost savings of £230,000 in England and £160,000 in Scotland, Wales, and Northern Ireland.

Authors' conclusions
The authors concluded that tiotropium was a cost-effective alternative to ipratropium and salmeterol, and switching COPD patients from ipratropium and salmeterol to tiotropium led to considerable cost savings for primary care trusts.

CRD commentary
Interventions:
The authors justified their selection of the comparators, which were all recommended in UK treatment guidelines for COPD patients. The dosages were clearly reported.

Effectiveness/benefits:
A selective approach was used to identify the relevant sources of evidence. Randomised controlled trials are generally considered to be valid sources of data given their methodological strengths. The authors stated that all trials included tiotropium and that the patients’ characteristics were similar, but more details would have helped in judging the validity of the clinical evidence. The approach used to pool the data from these trials was not stated. No information on the other sources of data was provided. QALYs were an appropriate benefit measure as COPD has a strong impact on the quality of life and life expectancy. The utility values were derived from a published study that included patients with COPD.

Costs:
The categories of costs reflected the viewpoint and it appears that no relevant item was excluded. The resource use was not presented separately from the unit costs, but the details of the costs associated with each health state and with exacerbations (mild versus severe) were reported. The use of a Delphi panel instead of real data for most of the resource use data was a potential limitation of the analysis, as acknowledged by the authors. The impact of variation in
these measures was extensively investigated. The price year was explicitly reported.

**Analysis and results:**
The approach used to analyse the results was appropriate and the incremental analysis allowed the identification of the most cost-effective strategy. The results were clearly reported. The issue of uncertainty was satisfactorily investigated, in several types of analysis (probabilistic, subgroup, etc). The authors justified the stochastic distributions chosen. The results of this analysis should be considered to be specific to the two settings.

**Concluding remarks:**
The methods were valid and the extensive analysis of uncertainty enhances the validity of the authors’ conclusions.

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