Evaluating the cost-effectiveness of tiotropium versus salmeterol 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.

CRD summary
This study examined the cost-effectiveness of tiotropium versus salmeterol for the treatment of patients with moderate chronic obstructive pulmonary disease. The authors concluded that, from the perspective of the third-party payer, tiotropium was more cost-effective than salmeterol or no treatment in patients with moderate disease. The cost-effectiveness framework was conventional, but the results were highly uncertain and the authors’ conclusion should be treated with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of tiotropium versus salmeterol for the treatment of patients with moderate chronic obstructive pulmonary disease (COPD) and a mean age of 65 years.

Interventions
The three interventions were tiotropium a long-acting anticholinergic (18 micrograms daily), salmeterol a long-acting beta agonist (50 micrograms twice daily), and no treatment. Treatment was assumed to last a maximum of one year and patients who discontinued treatment received maintenance therapy that consisted of ipratropium, albuterol, theophylline, and fluticasone.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a one-year time horizon and a hypothetical cohort of 100,000 male patients, with a mean age of 65 years, a smoking history of at least 50 pack-years (one pack-year defined as one packet per day for a year or the equivalent total over time), and a disease duration of at least 9.5 years. The authors stated that the analysis was conducted from the perspective of the third-party payer.

Effectiveness data:
A literature search was undertaken to identify the relevant clinical trials for the efficacy of the study drugs. Four placebo-controlled, randomised clinical trials were included, one of which provided head-to-head data for salmeterol versus tiotropium. The data for no treatment were from the placebo arms of the clinical trials. Other published studies were used for patients' compliance. The key input for the model was the efficacy rate.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of exacerbations (severe or not) was the benefit measure.

Cost data:
The economic analysis included the costs of drugs, hospitalisations, monitoring (laboratory tests), and physician visits. Conventional patterns of resource consumption were assumed. The drug costs and cost of maintenance therapy were based on average wholesale prices. All other costs were from Medicare sources. The costs were in US dollars ($) and the price year was 2006.

Analysis of uncertainty:
The uncertainty was investigated in a first-order Monte Carlo simulation, which assessed the variability around the mean outputs. A one-way sensitivity analysis focused on the following parameters: the probability of exacerbation, the probability of hospitalisation, the probability of severe exacerbation, and the compliance rate. The ranges of values were from the literature or were assumed to be ±20% of the baseline value.

Results
The total direct costs were $392.10 with no treatment, $1,268.66 with salmeterol, and $1,408.59 with tiotropium. The number of exacerbations avoided was 0.694 with no treatment, 1.052 with salmeterol, and 1.129 with tiotropium. Compared with no treatment, the incremental cost per exacerbation avoided was $2,454.48 with salmeterol and $1,817.37 with tiotropium. The authors excluded salmeterol on the grounds of extended dominance as it was less cost-effective than a more effective option (tiotropium).

The base-case findings changed dramatically with different assumptions on compliance. Lower compliance generally favoured salmeterol. For example, with 100% compliance for each treatment (90% for tiotropium and 75% for salmeterol in the base case), the incremental cost per exacerbation avoided was $3,327.03 for salmeterol and $7,554.64 for tiotropium. If the compliance with tiotropium was 75%, salmeterol 75%, and no treatment 50% (compliance with inhaled medication for the relief of asthma rather than prevention), the incremental cost per exacerbation avoided was $2,451.06 for salmeterol and $7,361.94 for tiotropium.

Authors’ conclusions
The authors concluded that, from the perspective of the third-party payer, tiotropium was more cost-effective than salmeterol or no treatment in patients with moderate COPD.

CRD commentary
Interventions:
The authors justified their selection of the comparators. The advantage of both drugs over other COPD medications was that they were long-acting and required less frequent administration. Several studies had shown the superior clinical profile of tiotropium over salmeterol, but salmeterol was cheaper.

Effectiveness/benefits:
A comprehensive approach was used to identify the relevant sources of evidence for the model, but limited details of the methods and conduct of the literature review were provided. The use of clinical trials enhanced the validity of the clinical inputs, given the methodological strengths of randomised controlled trials. The baseline characteristics of the patient population and the key results of the trials were reported, but the approach used to pool the data from these sources was not clearly stated and the authors did not address the potential heterogeneity of the sources. One trial included both salmeterol and tiotropium and it was unclear how the data from the other indirect comparisons were combined. The compliance was from a number of studies that were not fully described. The benefit measure was disease-specific and comparisons with the benefits of other health care interventions might not be possible. The impact of the treatments on health-related quality of life was not taken into account despite the substantial burden of disease for these patients.

Costs:
The categories of costs and their sources were consistent with the perspective stated. The unit costs were reported for all items, but no clear information was provided on resource consumption, which appears to have been from standard Medicare sources. The cost estimates were treated deterministically and alternative assumptions were not considered, but wide ranges of values were tested in the sensitivity analyses. The price year was clearly stated, allowing reflation exercises for other time periods.
Analysis and results:
Average and incremental analyses were used to synthesise the costs and benefits of the strategies and the projected costs and benefits were clearly presented. The uncertainty was investigated, using a probabilistic approach, but based on a first-order rather than a second-order Monte Carlo simulation, which would have provided more information on the variation in the model parameters. The results were strongly dependent on the assumptions for compliance. The authors compared their results with those from other published studies and stated that several methodological differences were found. These findings might not be transferable to other settings.

Concluding remarks:
The cost-effectiveness framework was conventional, but the results seemed to be highly uncertain. The authors’ conclusion should be treated with caution.

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