Cost-effectiveness of formoterol and salbutamol as asthma reliever medication in Sweden and in Spain


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
Two treatments for the relief of asthma, formoterol Turbuhaler 200 microg and salbutamol 200 microg, were examined.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 6 years or older with a wide range of asthma severity, who were taking various maintenance medications.

Setting
The setting was primary care. The economic study was carried out in Spain and in Sweden.

Dates to which data relate
The period during which the effectiveness and resource use data were gathered was not reported. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Overall, a sample of 18,124 patients was enrolled in the primary trial. There were 9,064 patients (57% female) in the formoterol group and 9,060 (58% female) in the salbutamol group. The mean age of the patients was 39 years (Age range: 5 - 91) in the formoterol group and 39 years (Age range: 4 to 91) in the salbutamol group. However, the sample of patients included in the current pharmacoeconomic evaluation comprised 17,618 patients, of which 8,786 were in the formoterol group and 8,832 in the salbutamol group.
Study design
This was a prospective, open-label, parallel-group, randomised trial that was carried out at 1,139 centres in 24 countries. The length of follow-up was 6 months. Patients attended the clinic at study entry and after 1, 3 and 6 months of treatment. Data on loss to follow-up were not reported.

Analysis of effectiveness
Several clinical outcomes were used in the primary trial, but the current analysis focused on severe or mild exacerbations (reported both separately and aggregated), symptom-free days, and the number of days with inability. A severe exacerbation was defined as one of the following asthma-related events: a hospitalisation, an emergency treatment, or a course of oral corticosteroids for at least 5 days. A mild exacerbation was defined as an increase in maintenance medication due to asthma. The numbers of symptom-free days were recorded during 2 weeks prior to visits 2, 3 and 4, and then extrapolated for the entire duration between two study visits. The number of days with inability to conduct normal activities (e.g. work) due to asthma for at least 6 hours was recorded. For children under the age of 12 years, the number of days that their parent or legal guardian was unable to conduct normal activities due to the child's asthma was recorded. Clinical data were self-reported, being registered in a specific notebook. The baseline comparability of the study groups was not discussed. The analysis of the clinical study appears to have been based on all patients included in the study sample.

Effectiveness results
The rate of severe exacerbations per year was 0.63 (+/- 2.69) with formoterol and 0.74 (+/- 4.00) with salbutamol (difference -15%; p=0.034).

The rate of mild exacerbations per year was 0.78 (+/- 2.19) with formoterol and 0.90 (+/- 2.29) with salbutamol (difference -13%; p<0.001).

The rate of total exacerbations per year was 1.41 (+/- 3.91) with formoterol and 1.64 (+/- 5.06) with salbutamol (difference -14%; p<0.001).

The percentage of symptom-free days was 58.82 (+/- 33.33) with formoterol and 57.20 (+/- 34.30) with salbutamol (difference 3%; p=0.0015).

The number of days with inability per year was 2.27 in the formoterol group and 2.51 in the salbutamol group (difference -10%; p=0.17).

Clinical conclusions
The effectiveness analysis showed that better outcomes were associated with formoterol treatment. Specifically, fewer exacerbations and more symptom-free days were achieved in comparison with salbutamol.

Measure of benefits used in the economic analysis
The summary benefit measures used were the number of severe exacerbations and the number of any exacerbations.

Direct costs
The analysis of the costs was performed from the perspective of the health care system, thus only the direct medical costs were included. The cost categories considered were study medications, maintenance medications for asthma, hospitalisations, emergency department visits, and other health care contacts. A breakdown of all medications used was given. The unit costs were reported separately from the quantities of resources used for most items. Resource use was estimated alongside the clinical trial. The costs were country-specific and were estimated using local experts and official statistics. Discounting was not relevant as the costs were incurred during 6 months. The price year was 2000.
Statistical analysis of costs
Cost-differences were tested using the parametric t-test.

Indirect Costs
The indirect costs were not included in the economic analysis.

Currency
Euros (EUR).

Sensitivity analysis
Sensitivity analyses were not carried out.

Estimated benefits used in the economic analysis
See the Effectiveness Results.

Cost results
The cost analysis showed a trend toward fewer resources used in the formoterol group, with the largest difference found for the number of hospital days and the number of emergency department visits.

In Sweden, the total daily costs per patient were EUR 2.49 with formoterol and EUR 2.35 with salbutamol (difference 6%).

In Spain, the total daily costs per patient were EUR 2.03 with formoterol and EUR 1.69 with salbutamol (difference 20%).

This suggests that the extra cost of formoterol was partly offset by reductions in cost as a result of lower use of other resources.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.

In Sweden, the incremental cost per avoided severe exacerbation with formoterol in comparison with salbutamol was EUR 1.38 per day (confidence interval, CI: 0.26 to 6.13) or EUR 504 per year (CI: 95 to 2,239). The incremental cost per any avoided exacerbation was EUR 0.62 per day (CI: 0.11 to 1.57) or EUR 140 per year (CI: 40 to 573).

In Spain, the incremental cost per avoided severe exacerbation with formoterol in comparison with salbutamol was EUR 2.98 per day (CI: 1.57 to 9.69) or EUR 1,088 per year (CI: 537 to 3,559). The incremental cost per any avoided exacerbation was EUR 1.34 per day (CI: 0.77 to 2.53) or EUR 489 per year (CI: 281 to 924).

Authors' conclusions
Formoterol, compared with salbutamol, as reliever medication produced statistically significant improvements in effectiveness (i.e. exacerbations and symptom-free days), less use of reliever and maintenance medication, and reduced resource use, with no increase (in Sweden) or only a limited increase (in Spain) in health care cost.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators selected for the analysis, which appear to have been appropriate. The dosages were reported. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data were obtained from a published study, thus few details were reported in the current pharmacoeconomic study. The use of a clinical trial was appropriate for the study question, and the randomised design ensures a high internal validity. A further strength of the analysis was the large sample of patients and the fact that evidence came from multiple institutions in different countries, which means that the study sample should have been representative of the patient population. Details of follow-up and baseline comparability of the study groups were not reported and, in general, an objective assessment of the robustness of the analysis was difficult. Nevertheless, the authors stated that the RELIEF study met the necessary quality requirements for a reliable cost-effectiveness analysis, suggesting a high internal validity of the analysis.

Validity of estimate of measure of benefit
The summary benefit measures were specific to the disease considered in the study. They would not be comparable with the benefits of other health care interventions. The impact of the interventions on quality of life was not assessed, but the number of exacerbations is commonly used in economic evaluations of asthma treatments.

Validity of estimate of costs
The cost analysis was consistent with the perspective adopted. The unit costs and the quantities of resources used were provided for most items, which enhances the possibility of replicating the analysis of costs in other settings. Two different analyses were carried out since country-specific costs were used. Limited information on the sources of the costs was provided. Resource use reflected actual treatment patterns in several countries. Traditional statistical analyses of the costs were carried to assess the significance of cost-differences, but the cost estimates were specific to the study setting. Sensitivity analyses were not carried out. The price year was reported, which means that reflation exercises in other settings are possible. The authors noted that the potential inclusion of indirect and intangible costs would have favoured the formoterol group, thus reducing or eliminating the cost-difference between the groups.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were not carried out, and the economic study focused on the two countries examined in the analysis. The study referred to patients with asthma and this was reflected in the authors’ conclusions.

Implications of the study
The study results support the use of formoterol as a relief medication in patients with asthma in Sweden. The indication for formoterol is less clear in Spain where the medication is associated with an extra cost from the perspective of the health care system.

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Other publications of related interest


Berggren F, Ekstrom T. A cost-effectiveness study comparing the as-needed use of formoterol (Oxis) and terbutaline (Bricanyl) in patients with moderate to severe asthma. Respir Med 2001;95:753-8.

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