Cost-effectiveness of eformoterol Turbohaler versus salmeterol Accuhaler in children with symptomatic asthma

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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 use of eformoterol, 12 microg twice daily (b.i.d.), for the treatment of paediatric asthma was examined.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children aged 6 to 17 years with a clinical diagnosis of asthma, who were treated with short-acting beta2-agonists and an inhaled corticosteroid.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
No dates were reported for effectiveness and resource use. In the budget impact analysis, the studies used to derive demographic and epidemiologic data were published between 1997 and 2000. The price year was 2000.

Source of effectiveness data
The effectiveness data in the main analysis were derived from a single study (published separately). Published data were used to conduct the budget impact analysis.

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

Study sample
Power calculations to determine the sample size were not performed. Also, the method used to select the sample was not reported. An overall sample of 145 patients was enrolled in the study. There were 73 children included in the eformoterol group and 72 children in the salmeterol group. The mean age of the children in the eformoterol group was 11.6 (+/- 3) years and 60% were boys. The mean age in the salmeterol group was 11.8 (+/- 2.8) years and 50% were boys.
Study design
This was a randomised, prospective, open-label, parallel trial that was carried out in several general practices in the UK and the Republic of Ireland. However, only patients enrolled in the UK were included in the analysis. The method of randomisation was not reported. The patients were followed for 12 weeks and assessment took place at weeks 4, 8 and 12. Four patients were lost to follow-up.

Analysis of effectiveness
The basis for the analysis was intention to treat. Patients who withdrew early through lack of effect or an adverse event were considered as failures. The primary health outcome assessed in the effectiveness analysis was the percentage of symptom-free days with no short-acting beta2-agonists. This was defined as days on which both the day- and nighttime symptom scores were recorded as zero, no nocturnal awakenings due to asthma were recorded, and short-acting beta2-agonist use was recorded at zero. The study groups were shown to be comparable at baseline, but there was a higher proportion of males in the eformoterol group than in the salmeterol group.

Effectiveness results
The mean percentage of symptom-free days with no short-acting beta2-agonists was 39% in the eformoterol group and 30% in the salmeterol group.

Clinical conclusions
The eformoterol-based treatment was more effective than the salmeterol therapy in increasing the number of symptom-free days.

Outcomes assessed in the review
The health outcomes used in the budget impact analysis were:

the percentage of the population aged 6 to 17 years,

the prevalence of Step 3 asthma in children aged 6 to 17 years according to the British Thoracic Society (entry criteria for the trial),

the average GP practice list size and the number of eligible children,

the average PCG population and the number of eligible children, and

the average HA population and the number of eligible children.

Study designs and other criteria for inclusion in the review
Most of the primary studies were official statistics published in the UK.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.
Number of primary studies included
The effectiveness data were derived from five primary studies.

Methods of combining primary studies
The studies were combined using narrative methods.

Investigation of differences between primary studies
Not carried out.

Results of the review
The percentage of population aged 6 to 17 years was 15.5%.

The prevalence of Step 3 asthma in children aged 6 to 17 years was 3.8%.

The average GP practice list size was 6,143 and 36 children were eligible.

The average PCG population was 105,808 and 615 children were eligible.

The average HA population was 498,961 and 2,898 children were eligible.

Measure of benefits used in the economic analysis
The mean percentage of symptom-free days with no short-acting beta2-agonists was the benefit measure used in the economic analysis. This was derived from the clinical trial.

Direct costs
No discounting was performed due to the short timeframe of the analysis (less than 1 year). The unit costs and the quantities of resources were reported separately. The costs included in the analysis were for the study drugs, short-acting beta2-agonists, unscheduled GP visits, severe exacerbation medications (oral corticosteroid courses) and relevant concomitant medications. The cost of hospitalisation was not included since no episodes of asthma-related hospitalised children were reported. GP visits due to the study protocol were considered atypical and were excluded from the analysis. The cost/resource boundary adopted in the analysis was that of the NHS. The cost data were estimated from published official sources for both drugs and personnel. Data on resource use were gathered prospectively during the clinical trial for all patients, irrespective of clinical trial completion. The price year was 2000.

Statistical analysis of costs
Standard statistical analyses were performed to compare the estimated costs in the base-case analysis.

Indirect Costs
The indirect costs were not included.

Currency
UK pounds sterling (€).

Sensitivity analysis
The robustness of the estimated costs and benefits to two alternative effectiveness measures were assessed using two
one-way sensitivity analyses. The effectiveness measures were the use of symptom-free days (defined earlier) and successfully controlled days. A successfully controlled day was specified as a peak expiratory flow of greater than 80% of baseline, less than 4 inhalations of short-acting beta2-agonists above baseline, and no nocturnal awakening. Non-parametric bootstrap replications were performed to assess the uncertainty around the incremental cost-effectiveness ratios (ICERs).

Estimated benefits used in the economic analysis
The mean percentage of symptom-free days with no short-acting beta2-agonists was 39% in the eformoterol group and 30% in the salmeterol group. This was estimated in the effectiveness analysis.

Cost results
The total per patient daily costs were 1.15 (standard deviation, SD=0.22; range: 0.85 - 1.97; 95% confidence interval, CI: 1.11 - 1.21) in the eformoterol group and 1.39 (SD=0.35; range: 0.98 - 2.53; 95% CI: 1.32 - 1.47) in the salmeterol group.

The eformoterol-based treatment saved 0.24 per patient. The difference was statistically significant, (p<0.001).

Synthesis of costs and benefits
The costs and benefits were combined using average and incremental cost-effectiveness analyses.

The average cost per symptom-free day with no short-acting beta2-agonists was 2.97 in the eformoterol group and 4.69 in the salmeterol group.

The estimated ICER of eformoterol over salmeterol was negative. This means that the eformoterol-based treatment was dominant, as it resulted in lower costs and greater effectiveness.

The bootstrap analysis showed that eformoterol was dominant in 96.6% of the cases.

The estimated ICER was robust to the variations in the effectiveness measure.

The budget impact analysis showed the expected annual costs were:
per patient, 421.14 for eformoterol and 507.03 for salmeterol (difference: 85.89) in children aged 6 to 17 years;
15,161 for eformoterol and 18,253 for salmeterol (difference: 3,092) for an average GP practice list;
259,004 for eformoterol and 311,826 for salmeterol (difference: 52,822) for an average PCG population; and
1,220,476 for eformoterol and 1,469,385 for salmeterol (difference: 248,909) for an average HA.

Authors’ conclusions
From the perspective of the UK NHS, the eformoterol-based treatment was more effective and less costly than salmeterol therapy for the treatment of paediatric asthma.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The authors stated that salmeterol represented a widely used treatment for paediatric asthma and the only long-acting beta2-agonist licensed for use in children before the introduction of eformoterol. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a multi-centred, randomised controlled trial, which was appropriate for the study question. It should ensure high validity in terms of the effectiveness results. The basis of the analysis was intention to treat, and the length and loss to follow-up were reported. However, power calculations and the method of randomisation were not reported, although details of the effectiveness analysis were published in a different article. The study groups differed at baseline in terms of the age of the children enrolled, which may have influenced the results. No formal review of the literature was undertaken for the budget impact analysis, but this was probably not necessary as the analysis was mainly based on data published by the Office of National Statistics and the Department of Health.

Validity of estimate of measure of benefit
The authors justified and discussed the use of the benefit measure selected in the economic analysis. Two sensitivity analyses were performed using two different benefit measures, to reflect the uncertainty around the choice of the most appropriate benefit measure.

Validity of estimate of costs
The analysis of the costs was conducted from the perspective of the NHS, and all the relevant categories of costs were included in the study. The authors justified the exclusion of some of the cost components, and it would appear that their omission should not affect the study results. The unit costs and the quantities of resources were reported separately. The price year was appropriately given. Statistical analyses were performed in the base-case analysis. The authors stated that no sensitivity analyses were conducted on the costs, as the main component of the cost analysis was the price of the drugs, which are fixed in the primary care setting in UK. The calculation of impact on the budgets at the GP practice, PCG and HA was a particularly useful approach and should assist UK decision-makers.

Other issues
The authors compared their findings with those from other studies. In terms of generalisability, the authors stated that the applicability of the study results to other settings should be assessed with caution, due to the variability of costs and management practice across countries. However, the fact that the details of the analysis were clearly reported, especially the cost analysis, enhances the degree to which it should be possible to reproduce the study in other settings. The study enrolled children with asthma defined according to the British Thoracic Society, and this was reflected in the conclusions of the analysis.

Implications of the study
The authors stated that further research should be carried out. This should involve a study with a longer time horizon and a larger sample size, to confirm the study results and generalise them to the general study population of patients with paediatric asthma.

Source of funding
None stated.

Bibliographic details

PubMedID
12000004

Other publications of related interest
Everden PR, Manion V, Reynia S, on behalf of the FACT Study Investigators’ Group. Formoterol Turbuhaler reduces the need for relief medication in children with mild to moderate asthma and improves quality of life. Eur Respir Med 2001;18 Suppl 33:291S.
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Subject indexing assigned by NLM

MeSH
Adolescent; Adrenergic beta-Agonists /economics /therapeutic use; Albuterol /analogs & derivatives /economics /therapeutic use; Asthma /drug therapy; Child; Cost-Benefit Analysis; Drug Costs; Ethanolamines /economics /therapeutic use; Female; Formoterol Fumarate; Great Britain; Humans; Male; Nebulizers and Vaporizers /economics; Primary Health Care /economics; Salmeterol Xinafoate

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