The cost-effectiveness of inhaled fluticasone propionate and budesonide in the treatment of asthma in adults and children

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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 health technologies were the use of fluticasone propionate (FP) and budesonide (Bud) in the treatment of patients suffering from asthma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of adult and paediatric patients suffering from asthma of all severities.

Setting
The setting was hospital. The economic analysis was carried out in the United Kingdom.

Dates to which data relate
Clinical and resource use data were obtained from studies published between 1994 and 1997. The price year was 1995.

Source of effectiveness data
The evidence for the final outcomes was based on a review of the literature.

Modelling
To perform the meta-analysis on the mean morning peak expiratory flow rate (PEFR), each separate trial was analysed with all patients included and using a common model involving centre, baseline and treatment factors (SAS Proc GLM (PC Version 6.08)). Similarly, in the meta-analysis for the plasma cortisol, each separate trial was analysed using the logarithm of the "end-treatment plasma cortisol as the response variable with centre, logged baseline and treatment factors included in the model". As the analysis includes all world-wide studies performed at a ratio of at least 1:2, a fixed-effect model was used for the meta-analysis.

Outcomes assessed in the review
The outcome measures were mean morning PEFR as the measure of efficacy and mean changes in serum cortisol as the measure of safety.
Study designs and other criteria for inclusion in the review
All studies comparing Bud with FP at half, or less than half, of the dosage of Bud, which included daily morning PEFR as an outcome measure in patients with asthma, and which were completed before December 1995, were included in the clinical meta-analysis. In each of the seven studies identified, all patients recorded morning PEFR, severity of daytime and night-time asthma symptoms, use of rescue bronchodilator medication and the incidence of exacerbation’s each day on a diary card during the run-in and treatment periods. The total number of patients was 1,980 (1,000 treated with FP 200-800 microg per day and 980 with Bud 400-1600 microg per day).

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
The criteria used were not systematically reported; it was only reported that data from the intention to treat populations from all the studies were used in the statistical analyses.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 7 studies (all studies were controlled, with 6 being open-label and one being double-blind) were included in the review.

Methods of combining primary studies
Meta-analysis was used to combine the primary studies. A pooled weighted mean of all the separate estimates of the treatment differences from each individual trial was calculated using the inverse variance from each trial as weights.

Investigation of differences between primary studies
No evidence was found for any heterogeneity among the estimates of morning PEFR or cortisol.

Results of the review
FP significantly improved mean morning PEFR compared with Bud, with an overall difference of +11 l/minute (95% CI: +7 - +15). In terms of mean changes in serum cortisol levels, no significant inter-group differences in serum cortisolos were detected at low doses. However, significant differences in favour of FP were apparent at higher dose levels (FP greater than 500 microg per day and Bud greater than 1200 microg per day). The pooled analysis also revealed a significant difference in cortisol ratios favouring FP (ratio = 1.09 nmol/l; 95% CI: 1.03 - 1.15).

Measure of benefits used in the economic analysis
Four measures of benefits were pre-determined for economic analysis. For improvements in lung function, two success criteria were defined: an increase in mean morning PEFR of greater than or equal to 15 l/minute between pre- and end-of-treatment; and a successfully treated week, defined as a week in which there was an improvement in mean morning PEFR of greater than or equal to 5% from baseline. For consistency, the end-of-treatment values used in these lung function-based measures of effectiveness were taken as the mean of the 7 days that ended 3 days before the last day of intended treatment. For symptom control, the measure was symptom-free day defined as a 24 hour period without any asthma symptoms being experienced by the patient, as recorded on the daily diary card. For management of symptoms and exacerbation’s, the episode-free day was used.
Direct costs
Costs were not discounted due to the short time frame of the cost analysis. The resource use profile was not reported separately from the costs. Cost breakdown was reported separately. The cost analysis covered the costs of study drugs, rescue medication, treatment of adverse events, and health-care contacts. Total direct health care costs of treatment were calculated by applying published unit costs to health care resource use reported during the studies. Resource use was identified from data recorded by the patient in the daily diary card (relief medications), and by the investigator in the concurrent medication forms and serious adverse event forms. A patient withdrawing early from the study was assumed to continue using resources at the same rate used in the time up to withdrawal, but to incur no further treatment benefits. Information on primary care and emergency room visits had not been recorded in any of the studies; assumptions were made regarding these resource use items. The price year was 1995.

Indirect Costs
Indirect costs were not considered.

Currency
UK pounds sterling (GBP).

Sensitivity analysis
One-way sensitivity analyses were performed on the threshold for success for the effectiveness measures based on lung functioning and on hospitalisation days for patients from whom the length of hospital stay was not recorded.

Estimated benefits used in the economic analysis
In this economic evaluation, a significantly higher number of patients receiving FP (49%) experienced a minimum improvement in mean morning PEFR of greater than or equal to 15 l/minute compared with 41% of those receiving Bud, (p<0.001). For the other lung function measure, the mean proportion of successfully treated weeks was 41.70% for FP, compared with 34.1% for Bud, (p<0.001). Assessing asthma symptom control, the mean percentage of symptom-free days was 41.7% for FP and 38.20% for Bud, (p=0.036). For control of symptoms and exacerbation's and the absence of adverse events, the proportion of episode-free days was 31% for FP and 26.7% for Bud, (p<0.003).

Cost results
The mean costs of treatment for FP were 7.78 per week and for Bud 12.33 per week.

Synthesis of costs and benefits
Although there was no methodological requirement for cost-effectiveness measures (as the use of FP was the dominant strategy), the authors reported four mean cost-effectiveness ratios:

- cost per improvement in mean morning PEFR greater than 151 mm - over study period, 2.55 for FP and 5.51 for Bud;
- cost per successfully treated week, 19.45 for FP and 41.20 for Bud;
- cost per symptom-free day (24 hour period), 2.79 for FP and 4.64 for Bud;
- cost per episode-free day, 4.23 for FP and 7.31 for Bud.

It was reported that across all variations of the sensitivity analysis, treatment with FP remained cheaper overall (and hence more cost-effective) than Bud.

Authors' conclusions
The study results demonstrate that, for asthma patients requiring modification of therapy, treatment with fluticasone propionate is more effective and also cheaper, in terms of overall health-care costs, than treatment with budesonide.

CRD COMMENTARY - Selection of comparators
The study appears to have adopted no comparator as both study drugs were deemed to be commonly prescribed. You, as a database user, should consider which strategy is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results is likely to be high due to the sound methodology adopted in combining the primary studies and the inclusion of world-wide trials. As mentioned by the authors, limitations of the analysis focus on the fact that some of the studies were open-label, because of difficulty in obtaining placebo devices for Bud. However, it is noteworthy that the double blind, double-dummy study significantly favoured FP, both in terms of efficacy and safety, and reflected the pooled analysis result. Some other limitations of the study were lack of information on sources searched for primary studies, criteria used to ensure the validity of primary studies, and methods used to judge relevance, validity, extracting data.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis. This choice of estimate was justified.

Validity of estimate of costs
The following features of the cost analysis are likely to have enhanced its validity: details of methods of cost estimation were given; the price year, and perspective adopted in the cost analysis were reported; unit costs appear to have been based on actual costs. However, the following features of the analysis may have weakened the validity of the cost analysis: the effects of alternative treatment strategies on indirect costs were not addressed; and no sensitivity analysis was performed on cost data.

Other issues
The authors' conclusions appear to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was addressed by noting that using published economic results for decision-making in a local setting requires not only assessments of the quality and relevance of the evidence, but also estimates of the costs and effectiveness likely to be seen locally rather than in the clinical trial setting, and judgement over the relative importance or value of the improvements in effectiveness. Comparisons were made with other studies. As asthma is a chronic condition, a cost-utility framework would have been a more appropriate approach for performing economic analysis.

Implications of the study
In interpreting these multiple endpoints choice of asthma therapy in a local setting, the decision-maker needs to evaluate to what extent the range improvements in the different outcomes are worth overall. With the cost savings shown in this study, the results suggest that this will be straightforward: improvements in asthma management can be achieved in parallel with reductions in cost.

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Other publications of related interest
Barnes N C, Hallett C, Harris T A J. Clinical experience with fluticasone propionate in asthma: a meta-analysis of efficacy and systemic activity compared with budesonide and beclomethasone dipropionate at half the microgram dose or less. Respiratory Medicine 1998;92:95-104.

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