Hydrofluoroalkane-134a beclomethasone as a dominant economic asthma therapy

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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
Two treatments for patients with persistent asthma were examined. The treatments were two widely used inhaled corticosteroids, hydrofluoroalkane beclomethasone (HDP-BDP) (QVAR) and chlorofluorocarbon beclomethasone (CFC-BDP) (Vanceril).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with persistent asthma.

Setting
The setting of the study was primary and secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from a single study, which was published in 2001 (see Other Publications of Related Interest). The price year was 2001.

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

Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of patients who participated in the effectiveness study.

Study sample
The use of power calculations was not reported. Patients enrolled at US sites within the multi-country clinical trial were included in the current analysis. Overall, 291 patients were identified, 218 in the HFA-BDP group and 73 in the CFC-BDP group. In the HFA-BDP group, the mean age was 36.4 (+/- 13.4) years and 70.2% were women. In the CFC-BDP group, the mean age was 35.4 (+/- 13.1) years and 70% were women. It was not stated whether some patients were excluded from the initial study sample for any reason. Authors' comment: no patients were excluded except for those outside of the USA.
**Study design**
This was a prospective, randomised, open label multicentre trial. The patients were randomised in a 3:1 ratio. The outcomes were assessed at baseline and 2, 4, 8 and 12 months, and daily diaries were used to report relevant episodes. The rates of study completion were 85.3% in the HFA-BDP group and 82.2% in the CFC-BDP group. The authors stated that patients withdrew from the study due to personal reasons (4.1%), noncompliance with the study protocol (3.4%), or they were lost to follow-up (2.4%). More information on the design of the trial was provided in the original publication (which referred to the whole sample of patients).

**Analysis of effectiveness**
The intention to treat principle was used in the analysis of effectiveness. The primary outcome measures were:

- the change in forced expiratory volume in 1 second,
- the median percentage change in symptom-free days (SFDs) from baseline to 12 months, and
- the median number of SFDs per patient.

An SFD was defined as a day without asthma symptoms. The study groups were shown to have been comparable at baseline in terms of their gender, age, lung function and tobacco use.

**Effectiveness results**
The median change in FEV1 from baseline to the 12-month assessment was 1.35% (mean 2% +/- 9.8) in the HFA-BDP group and 0% (mean 0.2% +/- 10.8) in the CFC-BDP group, (p=0.14).

The median change in SFDs from baseline to the 12-month assessment was 22.1% (mean 14.01% +/- 30) in the HFA-BDP group and 14.3% (mean 5.53% +/- 30.4) in the CFC-BDP group, (p=0.03).

The median number of SFDs per patient per year was 163.9 with HFA-BDP and 110.3 with CFC-BDP. The difference was 53.6 (49%).

**Clinical conclusions**
The effectiveness study showed that significantly more SFDs were achieved in HFA-BDP patients than in CFC-BDP patients suffering from persistent asthma.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the annual number of SFDs associated with each treatment. The benefit measure was obtained directly from the clinical trial.

**Direct costs**
Discounting was not relevant since the costs were incurred during 12 months. The unit costs and the quantities of resources used were presented separately. The health services included in the economic analysis were study medications, hospitalisations and urgent medical care visits. Routine physician visits were not considered, whereas all asthma and asthma-related medications were. Cost of exacerbation related visits were included. The cost/resource boundary of the MCO was adopted. Resource use was derived from actual data estimated alongside the clinical trial that provided the effectiveness evidence. It was estimated that the actual consumption of multidose packages reflected the true consumption of resources. The costs were obtained from an MCO with over 1 million enrollees and from average wholesale prices (medications). Common Procedural Terminology codes were used and reported for each item. The price year was 2001.
Statistical analysis of costs
The Wilcoxon rank sum test was used to test the statistical significance of differences in the estimated costs. The cost categories were presented as median and mean values with 95% confidence intervals (95% CIs).

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were conducted to investigate the robustness of the estimated costs and benefits of the interventions. The impact of using mean rather than median values for both the costs and effectiveness was investigated. The use of an alternative benefit measure (change in SFDs over time) or lower strength of HFA-BDP (40 microg instead of the 80 microg used in the base-case) was also investigated. The ranges used were derived from CIs.

Estimated benefits used in the economic analysis
As calculated in the effectiveness analysis, the median number of SFDs per patient per year was 163.9 with HFA-BDP and 110.3 with CFC-BDP. The difference of 53.6 (49%) favoured HFA-BDP.

Cost results
The estimated median total cost per patient was $667.68 (mean $891.35 +/- 607.76) with HFA-BDP and $977.05 (mean $1,173.95 +/- 642.30) with CFC-BDP, (p<0.001). Thus, HFA-BDP saved $309.37 (46%).

When the costs were broken down, only the difference in drug acquisition costs was statistically significant. The estimated costs were higher in the CFC-BDP group.

Synthesis of costs and benefits
The costs and benefits of the two alternative treatments were combined using average and incremental cost-effective ratios (ICERs).

The average cost per SFD was $4.07 with HFA-BDP and $8.86 with CFC-BDP.

The incremental analysis showed that HFA-BDP dominated CFC-BDP because it was more effective and less costly. The ICER with HFA-BDP relative to CFC-BDP was -$5.77 (95% CI: -68.08 - 4.08).

Using mean rather than median values did not change the conclusions of the analysis. Using the lower strength of HFA-BDP led to an ICER of -$1.13 (95% CI: -19.83 - 4.38). The ICER was -$40.20 when the change in SFDs over time was used as an alternative benefit measure. Changes in other factors did not lead to substantial variations in the dominance of HFA-BDP over CFC-BDP.

Authors' conclusions
Hydrofluoroalkane beclomethasone (HDP-BDP) was more cost-effective than chlorofluorocarbon beclomethasone (CFC-BDP) in the treatment of patients with persistent asthma.

CRD COMMENTARY - Selection of comparators
No explicit justification for the choice of the comparators was given. Both medications represented widely used
treatments for persistent asthma. However, the authors did not consider other available treatments. You should decide whether HFA-BDP and CFC-BDP are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a randomised trial, which was appropriate for the study question. Most of the details on the design and methods of the study were reported in a separate paper, as the current analysis focused only on patients identified in US-sites. Thus, it would appear difficult to assess the internal validity of the analysis. The validity was likely to have been high due to several features of the study. For example, the randomised design, the baseline comparability of the study groups, the similar completion rate, and the intention to treat basis of the analysis of the clinical study. However, it would have been interesting to have known whether the sample size was appropriate for the study question. The authors noted that the study sample was likely to have reflected a population of patients in which asthma was well controlled.

Validity of estimate of measure of benefit
The summary benefit measure was derived from the effectiveness study. It was specific to the disease considered in the study and is hardly comparable with the benefits of other health care interventions. An alternative but similar benefit measure was also used.

Validity of estimate of costs
The authors reported explicitly the perspective that was adopted in the study. It appears that all the relevant categories of costs, including those associated with exacerbation related visits, have been considered. Routine physician visits were not included, but no justification for such an exclusion was provided. Information on the unit costs was reported separately from the quantities of resources used, which enhances the possibility of replicating the study. The source of the cost data was reported. Actual resource consumption was estimated. The price year was reported, which aids reflation exercises in other settings. Non-parametric statistical tests were conducted to deal with highly skewed cost data and to compare the estimated costs. The estimates were specific to the study setting.

Other issues
The authors compared their findings with those from other studies that evaluated the cost-effectiveness of inhaled corticosteroids. However, the issue of the generalisability of the study results to other settings was not addressed, which reduces the external validity of the analysis. Some sensitivity analyses were conducted. The statistical tests were appropriate given the skew in the cost data. The authors discussed some potential limitations of their analysis. The use of ICERs appears unnecessary given the dominance of HFA-BDP over CFC-BDP.

Implications of the study
The authors suggested that HFA-BDP is "worthy of adoption by health care payers in place of CFC-BDP".

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Other publications of related interest

**Indexing Status**
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**MeSH**
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