Health technology
Two treatments for asthma control were examined. One was a combination of salmeterol and fluticasone propionate (SFC), the other was fluticasone propionate alone (FP). A stepwise programme of increased dosages of SFC or FP was analysed.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients requiring further treatment for asthma control.

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

Dates to which data relate
The effectiveness and resource use data were derived from the GOAL study published in 2004. The costs were expressed at 2003/04 prices.

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
Power calculations were not reported. An overall sample of 3,416 patients was considered. The number of patients included in each treatment arm was not reported. The patients were stratified into three approximately equal groups and were allocated to the FP or SFC arms of the trial. The three strata related to the patients' use of inhaled corticosteroids for 6-months prior to screening for study entry. Stratum 1 corresponded to no inhaled corticosteroid. Stratum 2 corresponded to 500 microg or less of beclomethasone dipropionate (BDP), or equivalent. Stratum 3 corresponded to more than 500 microg to 1,000 microg or less of BDP, or equivalent.
Study design
This was a prospective, randomised, double-blind controlled trial that was carried out in 44 countries. The length of follow-up was 52 weeks. Other details of follow-up and blinding were not reported. The study comprised two phases. In the first phase, patients were in the dose-escalation phase where the dose of FP or SFC would be stepped up if they failed to achieve total control in at least 7 weeks of an 8-week assessment period. Patients then entered the second (maintenance) phase, where their dose remained at the level they reached at the end of the first phase.

Analysis of effectiveness
The primary outcome measure used in the analysis was asthma control. At the end of the follow-up period, the patients were classified into four control categories:
'totally controlled' (TC);
'well controlled' (WC);
'not well controlled' (NWC) but without exacerbation; and
'exacerbation' (X).
The TC and WC categories were defined on the basis of treatment guidelines. The categories of control status identified (above) were employed as the dependent variable in a multinomial regression model, to estimate the proportion of time patients spent in each category of control while adjusting for the baseline strata and treatment allocation of each patient. Health-related quality of life utilities were also estimated using the Asthma Quality of Life Questionnaire (AQLQ), which were translated into a utility score using a mapping algorithm. Thus, AQLQ scores were translated into utilities that were entered into a regression analysis that enabled the utility scores to be directly associated with control status categories. The baseline comparability of the study groups was not discussed, but it is likely that the treatment arms were similar given the randomised method used in the trial. The approach used to analyse the clinical outcomes (intention to treat or treatment completers only) was not stated.

Effectiveness results
The proportions of time spent in the various categories of control were as follows (category in parentheses).
Stratum 1 with FP: 32% (TC), 33% (WC), 34% (NWC) and 1% (X).
Stratum 1 with SFC: 40% (TC), 32% (WC), 28% (NWC) and 0% (X).
Stratum 2 with FP: 22% (TC), 31% (WC), 46% (NWC) and 1% (X).
Stratum 2 with SFC: 35% (TC), 34% (WC), 30% (NWC) and 1% (X).
Stratum 3 with FP: 17% (TC), 29% (WC), 52% (NWC) and 2% (X).
Stratum 3 with SFC: 26% (TC), 33% (WC), 40% (NWC) and 1% (X).
The data showed that combination treatment had a positive impact on asthma control in comparison with FP monotherapy, regardless of the baseline stratum of patients. Strata were all significant predictors of control status, (p<0.001).
The regression model provided a good fit to the observed data.
Weekly utilities were 0.946 (+/- 0.011) for TC, 0.900 (+/- 0.011) for WC, 0.842 (+/- 0.011) for NWC and 0.729 (+/- 0.013) for X.
The utility scores were also reported as the results of the regression model. An adjustment factor of 0.044 was used for
UK patients. Again, strata were all significant predictors of control status, (p<0.001).

**Clinical conclusions**
The effectiveness analysis showed that the combination therapy led to better asthma control than FP monotherapy.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the number of quality-adjusted life-years (QALYs). These were estimated by combining the proportion of time spent in each state with the quality of life in each state. No discounting was applied.

**Direct costs**
The analysis of the costs was carried out from the perspective of the NHS. It included three main categories of costs (secondary care visits, primary care visits and medication). Secondary care costs covered visits to emergency departments, length of time in the intensive care unit, outpatient visits, and inpatient days. Primary care costs consisted of general practitioner home visits during the day and the night, visits to the primary care clinic, and telephone calls to the primary care clinic. Information on medications used distinguished between study drugs and rescue medication use. Resource use was taken from the whole GOAL data series in order to maximise the power of the resulting analysis, but a UK indicator variable was employed in the regression model to adjust the analysis for UK-specific effects. The unit costs and the quantities of resources used were not presented separately. The unit costs were derived from published sources in the UK based on the Personal and Social Services Research Unit. Discounting was not relevant as the costs were incurred during a 1-year time horizon. The costs were expressed as 2003/04 prices.

**Statistical analysis of costs**
The total costs were estimated using standard regression analysis in order to estimate the costs separately for each stratum.

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

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
The issue of uncertainty was addressed through uncertainty in the estimated coefficients of each regression model. A non-parametric approach of bootstrapping was employed to account for potential correlation between the regression models comprising the analysis and to calculate confidence intervals (CIs) for the cost-utility ratios.

**Estimated benefits used in the economic analysis**
The total QALYs gained with SFC over FP were 0.0118 (95% CI: 0.0094 to 0.0143) for stratum 1, 0.0120 (95% CI: 0.0094 to 0.0145) for stratum 2 and 0.0118 (95% CI: 0.0093 to 0.0141) for stratum 3.

**Cost results**
The total additional costs associated with SFC over FP were 163 (95% CI: 147 to 177) for stratum 1, 132 (95% CI: 114 to 147) for stratum 2 and 90 (95% CI: 61 to 109) for stratum 3.

**Synthesis of costs and benefits**
An incremental cost-utility ratio was calculated to combine the costs and QALYs of SFC versus FP.

The incremental cost per additional QALY gained with SFC over FP was 13,700 (95% CI: 11,000 to 18,300) for stratum 1, 11,000 (95% CI: 8,600 to 14,600) for stratum 2 and 7,600 (95% CI: 4,800 to 10,700) for stratum 3.

Authors' conclusions
The use of salmeterol-fluticasone propionate (SFC) combined therapy compared with fluticasone propionate (FP) alone resulted in a cost-utility ratio that compared favourably with other uses of scarce health care resources in the UK, as the National Institute for Clinical Excellence has recently suggested.

CRD COMMENTARY - Selection of comparators
The choice of the two treatments was based on the objective of the GOAL study. Dosages of the stepwise programme were described. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from a clinical trial, which was appropriate for the study question. The clinical trial should have had a high internal validity since the randomisation approach would reduce selection bias. The large sample of patients recruited and the multinational design also increase the internal validity of the study. Moreover, the stratified design and the use of statistical analyses represented strong features of the analysis. However, the clinical trial had been published elsewhere, thus limited information on the methods of sample selection, randomisation and outcome assessment were available in the present paper.

Validity of estimate of measure of benefit
QALYs were an appropriate benefit measure because they capture the impact of the intervention on quality of life, which is likely to be relevant for patients with asthma. The analysis focused on quality of life aspects that were assessed using an asthma-specific instrument and converted to utility weights by means of an algorithm. QALYs are comparable with the benefits of other health care interventions. Discounting was not applied since the interventions had no impact on life expectancy.

Validity of estimate of costs
The costs included were consistent with the perspective adopted in the analysis. A detailed breakdown of the cost items was not given and information on the unit costs and resource quantities was not provided. This could limit the possibility of replicating the analysis in other settings. The cost estimates were specific to the study setting and were derived from typical UK sources. Variations in individual costs were not investigated in a sensitivity analysis, but a non-parametric approach was used to deal with the issue of uncertainty. Further, statistical analyses were carried out to link costs to baseline disease severity (stratum). The use of the whole data series of the trial for resource use, and the adjustment to UK patients by means of a regression model, appears to be a strong feature of the analysis. The price year was reported, which enhances the possibility of performing reflation exercises in other time periods.

Other issues
The authors did not compare their findings with those from other studies. The issue of the generalisability of the study results to other settings was not explicitly addressed, although an extensive sensitivity analysis was carried out to deal with the issue of uncertainty in the clinical and economic estimates. The authors noted that the whole data series was used for both clinical and economic data, although the analysis was restricted to the UK setting in order to increase the power of the analysis. The study referred to patients requiring further treatment to achieve asthma control, and this was reflected in the authors' conclusions.

Implications of the study
The study results support the use of SFC to improve asthma control.

**Source of funding**
Funded by GlaxoSmithKline.

**Bibliographic details**

**PubMedID**
16629780

**DOI**
10.1111/j.1398-9995.2006.01038.x

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Albuterol /analogs & derivatives /economics /therapeutic use; Androstadienes /economics /therapeutic use; Asthma /drug therapy /economics; Bronchodilator Agents /economics /therapeutic use; Cost-Benefit Analysis /methods /statistics & numerical data; Double-Blind Method; Drug Combinations; Fluticasone; Fluticasone Propionate, Salmeterol Xinafoate Drug Combination; Great Britain; Humans; Models, Statistical; Outcome Assessment (Health Care) /economics /methods; Quality of Life; Quality-Adjusted Life Years; Time Factors; Treatment Outcome

**AccessionNumber**
22006001360

**Date bibliographic record published**
30/11/2006

**Date abstract record published**
30/11/2006