Cost-effectiveness of inhaled corticosteroids in adults with mild-to-moderate asthma: results from the Asthma Policy Model

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 inhaled corticosteroid (ICS) therapy in treating asthma.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The hypothetical population was aged 18 years and over with mild to moderate asthma. Mild asthma was measured by FEV1 as 80-100% of predicted normal, and moderate as 60-80%.

Setting
The setting was community and based in the United States.

Dates to which data relate
The effectiveness data were derived from studies published between 1990 and 1999. Costs were estimated from resource utilisation studies published between 1984 and 1999. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
The model used was a Markov chain state-transition simulation. The disease states used were:

stable/chronic;
acute event - non-emergency department (ED) urgent care visits;
acute event - ED visits without hospitalisation;
acute event - hospitalisation;
death - asthma related; and
death - other causes.
The probability of transition between states depended on:

- age of patient (18-35 or 35+);
- severity of lung function impairment (mild or moderate); and
- number of prior hospitalisations (none, one, more than one).

The purpose of the model was to simulate the natural history of the disease for each treatment arm and to estimate benefits and costs for a cohort of patients over a 10 year planning horizon.

### Outcomes assessed in the review

The following outcomes were assessed in the review (as input parameters to the model):

- the relationship between lung function and symptom days;
- the relationship between lung function and observed rates of Emergency Department (ED) use;
- the relationship between ICS therapy and lung function, net of any placebo effect; and
- mortality from asthma and other causes.

### Study designs and other criteria for inclusion in the review

To estimate the effectiveness of ICS therapy a search of MEDLINE was undertaken using the following terms: 'randomized clinical trial', 'asthma', 'FEV1' (or synonyms) and 'beclomethasone' (or equivalents). The criteria used were: RCT with one arm as placebo, the intervention was an ICS therapy, FEV1% predicted was used as an outcome.

### Sources searched to identify primary studies

MEDLINE was searched to identify primary studies.

### Criteria used to ensure the validity of primary studies

Not stated.

### Methods used to judge relevance and validity, and for extracting data

The authors assumed equivalence across dose ranges for the ICS therapy studies.

### Number of primary studies included

Sixteen studies, yielding 26 active treatment arms, were included in the review. (There are 5 currently available ICS therapies in the US market).

### Methods of combining primary studies

The review calculated the mean change in FEV1% predicted, weighted by the number of study subjects (both for all studies combined and stratified by baseline lung function).

### Investigation of differences between primary studies

No investigation reported.
Results of the review
The relationship between lung function and symptom days:

\[ \% \text{ symptom days} = \frac{1}{1+\exp(-12.5 +0.1550 \times \text{FEV1} \% \text{ predicted})} \times 100. \]

The relationship between lung function and observed rates of Emergency Department (ED) use:

\[ \text{ED rate} = \frac{1}{1+\exp(-2.1872 + 0.0560 \times \text{FEV1} \% \text{ predicted})} \times 100. \]

The relationship between ICS therapy and lung function, net of any placebo effect:

ICS therapy produces baseline relative increases in FEV1% of 7.6% for patients with mild disease and 11.6% for patients with moderate disease.

Mortality from asthma:

monthly probability of asthma related death = 1\times10^{-5} for patients aged 18-35 and 2\times10^{-5} for patients aged 35+.

Measure of benefits used in the economic analysis
The benefit measures were: Quality-adjusted life-years (QALYs), symptom days, per-person acute exacerbation's and hospitalisations.

QALYs were determined using preference weights collected in a companion, cross sectional study of 100 adults with asthma in Kentucky USA. The baseline assessment used the time trade-off (TTO) method. Other methods were also used for sensitivity analysis (standard gamble and rating scale questions). The attributes used the Health Utilities Index and the Asthma Symptom Utility Index. Benefits were discounted at 3%. The authors estimated the relationship between Quality of life (time trade-off method) and lung function as:

\[ \text{TTO} = 0.521 + 0.003958 \times \text{FEV1} \% \text{ predicted}. \]

Direct costs
Costs were discounted at 3%. Costs and quantities were analysed separately. Costs were broken downs as: monthly chronic care costs (medications, routine office visits, laboratory testing), acute event costs (non-ED urgent care, ED visits and hospitalisations) and ICS therapy drug costs. The quantity/cost boundary adopted was not stated. Costs were estimated from published resource utilisation studies, using the model to derive expected resource use. The price year was 1998, adjusted where necessary using the medical care component of the US Consumer Price Index. The study did not state whether costs were average or marginal.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
Although the perspective was stated to have been societal, the authors did not include any indirect costs.

Currency
US dollars ($).

Sensitivity analysis
The following one-way sensitivity analyses were carried out:

effect of ICS therapy: from 1 to 22% of the baseline case;
costs: from 50% to 200% of baseline;

quality of life: alternative models (TTO, SG, rating scale);

side effects: a percentage across-the-board reduction in the HRQoL for ICS therapy of 0% (no side effect), 1%, 2% and 3%; and

length of analysis: reduce 10-year period of analysis to 5 years.

**Estimated benefits used in the economic analysis**
Patients in both arms lived 9.2 years on average, undiscounted and unadjusted for Health-related quality of life (HRQoL) effects.

The comparator strategy generated 1,051 symptom days, 4.5 acute episodes, 0.21 hospitalisations and 6.8 discounted QALYs per patient on average.

The ICS therapy strategy generated 622 symptom days, 3.0 acute episodes, 0.14 hospitalisations and 7.0 discounted QALYs per patient.

No side effects were considered in the baseline case analysis.

No confidence intervals were reported.

**Cost results**
The strategy of quick relievers plus ICS therapy cost $8,400 discounted over 10 years. The comparator strategy cost $5,200 discounted over 10 years. Non-discounted costs were not reported. The discount rate used was 3%. No statistical analysis was undertaken.

**Synthesis of costs and benefits**
The incremental cost/utility ratio was $13,500 per QALY gained, and $7.50 per discounted symptom-free day gained. An incremental analysis was performed comparing no ICS with a targeted ICS intervention for moderate asthma patients' only, mild asthma patients only and all patients. This showed the moderate asthma patients only strategy to be the most cost-effective ($10,300 per QALY) and increased the incremental cost/QALY for the strategy to treat all patients to $15,000 when compared with treatment of moderate asthma patients only.

As the efficacy of ICS therapy was varied from 1% to 22% of the baseline case the cost-effectiveness ratio ranged from $5,000 to $128,000. Varying the method used to elicit patient preferences varied the cost-effectiveness ratio from about $10,000 to about $45,000, though it was not stated which method gave which result. Varying the HRQoL by an across the board decrement of 3% to reflect side effects increased the cost-effectiveness ratio to $129,000.

**Authors' conclusions**
The authors concluded that ICS therapy offers good value for patients with both mild and moderate asthma. They compared ICS intervention with cost-effectiveness ratios for other life saving and health promotion activities from a league table. They recognised a number of limitations in the study. There was a wide range of estimated efficacy of ICS therapy. There was a lack of data on side effects of ICS therapy. The sources for cost data were varied and may reflect different patient populations. They viewed the model as a starting point to explore many questions about treatment of asthma.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of comparator was not explicit but it appears to have represented current practice.
Validity of estimate of measure of effectiveness
To estimate the effect of ICS therapy: the sources of the data were clearly identified and were selected by a systematic review. The methods and conduct of the review were satisfactorily reported. Effectiveness estimates were appropriately combined using a weighted average method. The authors recognised that side effects of treatment were handled in a speculative fashion, and that this affected the validity of the study. The estimate of effectiveness in the sources varied considerably. It should be noted that using the lowest estimate reversed the conclusion that the ICS therapy offered good value.

Validity of estimate of measure of benefit
Quality of life estimates were derived using a specially designed study of asthma patients, which enhances the validity of the results. Measures of benefit were modelled using a Markov-chain process, which was appropriate.

Validity of estimate of costs
No costs for time and productivity losses of adult asthma were included, which would be relevant for the stated perspective (societal). Therefore the study has not included all relevant costs in the analysis. This may have understated the cost-effectiveness of ICS if it is an effective treatment. Good features were that costs and quantities were reported separately for some categories of costs (use of ICS drugs, hospitalisations), and the price year was given, enhancing the generalisability of the results.

Other issues
The authors described the study as a cost-effectiveness analysis but, since it used QALYs, would more conventionally be described as a cost-utility analysis. The authors compared their baseline cost-effectiveness ratios with a 'league table' of treatments for other diseases to demonstrate cost-effectiveness of ICS therapy. Generalisability to other settings was not discussed in detail, but the authors considered the possibility that the model could be extended to the European setting or study children. The authors did not appear to have presented their effectiveness results selectively.

Implications of the study
The authors endorsed the use of ICS therapies for patients with both mild and moderate asthma. They noted the lack of evidence regarding side effects of ICS therapy and its impact on HRQoL, and suggested these as areas for research. They recommended that the Asthma Policy Model should be further refined to be used to assist priority setting in patient care.

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