Inhaled corticosteroids plus salmeterol or montelukast: effects on resource utilization and costs
Stempel D A, O’Donnell J C, Meyer J W

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 alternative treatments for patients with moderate persistent asthma were examined. The treatments were inhaled corticosteroids (ICSs) used concurrently with salmeterol (ICS+SAL) or montelukast (ICS+MON). A third comparator, inhaled fluticasone propionate plus SAL (FP+SAL), was also considered.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with moderate persistent asthma. All patients aged between 4 and 65 years, who had a primary medical claim for asthma (ICD-9, code 493.XX) and who were currently receiving ICSs, were eligible for inclusion. Patients with a diagnosis of cystic fibrosis were excluded. Patients could only have received either SAL or MON.

Setting
The setting was not reported. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data referred to 1996 to 1999. No price year was reported, but medical claims from 1997 and 1998 were used for the costing.

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

Link between effectiveness and cost data
The costing was performed retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not performed. All patients whose paid claims were identified during the study period were included in the analysis. An overall sample of 919 patients was considered, 703 in the ICS+SAL group and 216 in the ICS+MON group. The mean age in the ICS+SAL group was 40.5 (+/- 16.3) years and 61.5% of the patients were women. In the ICS+MON group, the mean age was 30.9 (+/- 19.8) years and 52.8% were
women. In the secondary analysis, the FP+SAL group comprised 261 patients. The mean age was 39 (+/- 17.1) years and 60.9% were women.

**Study design**
This was a retrospective cohort study, which is likely to have been conducted in a single centre. The analysis considered a 24-month period, 12 months before and 12 months after the index event, which was the first prescription of the therapies. All patients for whom an index event occurred between January 1997 and September 1998 were considered. No loss to follow-up was reported because only complete patient charts were selected.

**Analysis of effectiveness**
All of the patients included in the initial study were considered in the effectiveness analysis. The outcomes used were the number of patients with at least one asthma-related hospitalisation or ED visit, and the number of filled prescriptions for short-acting beta2-agonists (SABAs). In terms of the baseline comparability of the study groups, the patients in the ICS+MON group were younger, more likely to be female, and had higher pre-index asthma costs than those included in the ICS+SAL group. The authors carried out several statistical analyses to take such differences into account when estimating the effectiveness. In the secondary analysis, the baseline characteristics of the patients in the two groups were generally similar. However, those in the FS+SAL group were older and presented lower pharmacy costs than those in the ICS+MON group.

**Effectiveness results**
In the ICS+MON group, the number of patients with at least one asthma-related ED visit was 30 (13.9%) in the pre-index period and 28 (13%) in the post-index period. The corresponding numbers in the ICS+SAL group were 98 (13.9%) and 76 (10.8%) in the pre- and post-index periods, respectively. There was no statistically significant difference between the groups.

In the secondary analysis, the number of patients with at least one asthma-related ED visit was 45 (17.2%) in the pre-index period and 23 (8.8%) in the post-index period in the FP+SAL group. This was statistically significant in comparison with ICS+MON, (p=0.0421).

In the ICS+MON group, the number of patients with at least one asthma-related hospitalisation was 9 (4.2%) in the pre-index period and 10 (4.6%) in the post-index period. The corresponding numbers in the ICS+SAL group were 31 (4.4%) and 12 (1.7%) in the pre- and post-index periods, respectively. The risk of hospitalisation was 2.5-fold greater with ICS+MON than with ICS+SAL, (p=0.0656).

In the secondary analysis, the number of patients with at least one asthma-related hospitalisations was 12 (4.6%) in the pre-index period and 3 (1.1%) in the post-index period in the FP+SAL group. The risk of hospitalisation increased to 5-fold in comparison with ICS+MON, (p=0.0299).

The post-index SABA use was 3.29 canisters/year in the ICS+SAL group, 4.45 canisters/year in the ICS+MON group, and 2.79 canisters/year in the FP+SAL group, (p<0.001).

**Clinical conclusions**
The effectiveness analysis showed that ICS+SAL was more effective than ICS+MON in reducing the number of hospitalisations and ED visits. Better outcomes were also found with FP+SAL when compared with ICS+MON.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the analysis. A cost-consequences analysis was therefore conducted.
Direct costs
Discounting was not conducted since the costs per patient were incurred during two years. The unit costs were not analysed separately from the quantities of resources used. The health services included in the analysis referred to all asthma-related utilisation, but a detailed breakdown of the costs was not reported. The cost/resource boundary adopted in the study was not stated. The costs were estimated from individual provider claims with a primary or secondary ICD-9 code for asthma, facility claims with a primary ICD-9 code for asthma, and pharmaceutical claims coded as "Bronchodilators and related drugs". Resource use was estimated on the basis of patient claims for 1996 to 1999. No price year was reported.

Statistical analysis of costs
Statistical analyses were conducted to test the statistical significance of differences in the estimated total costs of the two treatments under evaluation. The method of ordinary least-squares regression was used. Covariates, such as demographics, prescriber specialty, and indication for chronic obstructive lung disease or other respiratory co-morbidities, were used to assess the impact of baseline factors on the estimated costs. Other statistical tests were carried out to deal with the skewed distribution of the costs.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The asthma pharmacy costs were $987 in the ICS+MON group and $606 in the ICS+SAL group.

The total asthma costs were $1,552 in the ICS+MON group and $952 in the ICS+SAL group.

The total health care costs were $4,346 in the ICS+MON group and $3,466 in the ICS+SAL group.

These figures were adjusted for the covariates considered in the analysis. All of the differences were statistically significant. Similar results were observed in the secondary analyses, where the costs were significantly lower in the FP+SAL group than in the ICS+MON group.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant because a cost-consequences analysis was conducted.

Authors' conclusions
The use of salmeterol (SAL) concurrently with inhaled corticosteroids (ICSs) led to reductions in hospitalisations, emergency department (ED) visits and the overall costs of treatment, compared with montelukast (MON) added to ICS. Similar results were obtained when SAL was administered concurrently with fluticasone propionate (FP).
CRD COMMENTARY - Selection of comparators
The authors did not explicitly justify the choice of the comparators, but ICS represented the therapy recommended by the National Institute of Health guidelines. As an adjunctive therapy, it was clear that SAL represented a widely used medication, which had been compared with MON in earlier randomised trials. A double dose of ICS could have been another relevant alternative. 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 cohort study and the data were gathered retrospectively. The use of a prospectively randomised design would have been more appropriate for the study question. The study sample was unselected and it appears to have been representative of the study population. Several issues limited the internal validity of the analysis. First, the size of the sample was not determined on the basis of power calculations. Second, the two groups were not well balanced at baseline, although the authors performed a regression analysis to adjust the final estimates. Third, the outcome measures did not directly reflect the impact of the treatments on patient health, but represented proxies for exacerbation episodes.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis so a cost-consequences analysis was conducted.

Validity of estimate of costs
There were very few details about the economic analysis. The perspective adopted in the study was not stated and a breakdown of the cost categories was not provided. In addition, the price year and the source of the cost data were not given. This makes the replication of the study in other settings difficult. Charges rather than costs were used and the cost estimates were specific to the study setting. These further limit the generalisability of the cost results. However, the authors conducted several statistical tests to consider the impact of confounding factors and variability in the data.

Other issues
The authors compared their findings with those from other studies and stated that their results confirmed those observed in the literature. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not conducted. These factors reduce the external validity of the analysis. The authors noted some limitations of the analysis. In particular, the use of an administrative database to gather effectiveness data, variation in the cost data, and the retrospective design.

Implications of the study
The study results and the evidence published in the literature suggest that SAL added to ICS may represent a reduction in asthma exacerbation and health care costs, compared with the use of MON.

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