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 technology was controller therapy for patients with asthma. The comparators were inhaled corticosteroids and leukotriene modifiers in real world clinical practice. The authors compared fluticasone propionate (44 or 110 microg) with oral zafirlukast (20 mg) and montelukast (5 or 10 mg).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population included patients that had a primary ICD-9-CM code (493.xxx) for asthma that occurred any time in the database. The patients were aged 4 years or older and had to have been enrolled in the plan continuously for at least 18 months, that is, 9 months before (preindex) and 9 months after (postindex) the first initial prescription. During the initial 9 months, the patients were required not to have had an inhaled corticosteroid or an oral leukotriene modifier. Patients were excluded if they had pharmacy claims for several drugs of interest, they were younger than 4 years or older than 45 years, and if they had had one or more prescriptions for ipratropium bromide during the study period. Patients with a diagnosis of cystic fibrosis or chronic obstructive pulmonary disease were also excluded.

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

Dates to which data relate
The effectiveness data were collected from 1 July 1997 to 30 June 1999. The dates to which the costs referred were unclear, although they appear to have been the same as those for the effectiveness data. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
It was not stated clearly whether the costing was undertaken on the same sample as that used in the effectiveness study. However, it appears that the costing has been undertaken retrospectively on the same sample.
Study sample
The sample size was not determined in the planning stages of the study. The sample was selected by collecting data for all patients with a primary ICD-9-CM code for asthma at anytime during the study period. Of the 781 patients included in the study, 284 were taking fluticasone propionate, 302 montelukast and 195 zafirlukast.

Study design
This was a multi-centre, retrospective cohort study. The data were collected over 2 years.

Analysis of effectiveness
The primary health outcomes used were emergency department visits and hospitalisations. The paper did not report whether any participants were excluded for incomplete data. The groups were comparable at baseline analysis.

Effectiveness results
The fluticasone propionate group had 3.5% preindex and 3.2% postindex emergency department visits, and 3.2% preindex and 1.8% postindex hospitalisations.

The montelukast group had 2.3% preindex and 3.0% postindex emergency department visits, and 1.7% preindex and 3.0% postindex hospitalisations.

The zafirlukast group had 4.6% preindex and 7.2% postindex emergency department visits, and 6.2% preindex and 6.7% postindex hospitalisations.

The logistic regression showed that patients who received zafirlukast had a 3.4 fold (95% confidence interval, CI: 1.1 - 10.7) greater risk of asthma-related hospitalisation compared with fluticasone propionate-treated patients. Those treated with montelukast had a 1.9 fold (95% CI: 0.6 - 6.2) increase in risk compared with those treated with fluticasone propionate.

Patients aged 12 years and older who received zafirlukast had a 3.7 fold (95% CI: 1.1 - 13-0) increase in risk of asthma-related hospitalisation compared with fluticasone propionate-treated patients. Those treated with montelukast had a 2.2 fold (95% CI: 0.6 - 8.4) increase in risk compared with those treated with fluticasone propionate.

Patients on zafirlukast had a 1.8 fold (95% CI: 0.7 - 4.9) increased risk of an asthma-related emergency department visit, compared with fluticasone propionate-treated patients, while those on montelukast had a 0.9 fold (95% CI: 0.3 - 2.6) decrease in risk.

Patients aged 12 years and older who received zafirlukast had a 2.6 fold (95% CI: 0.9 - 7.7) increase in risk of an asthma-related emergency department visit, compared with fluticasone propionate-treated patients, while those treated with montelukast had a 1.6 fold (95% CI: 0.5 - 5.0) increase in risk.

Logistic regression was not performed in the 4- to 11-year-old group, as there were too few hospitalisations or emergency department visits.

Significantly fewer patients in the fluticasone propionate group (7.4%, p<0.001) switched or added therapy compared with those in the montelukast (31.5%) and zafirlukast (42.6%) groups. Compared with the fluticasone propionate group, the risk of switching to another controller agent was 7.2 times higher in the zafirlukast group, (p<0.001), and 4.9 times higher in the montelukast group, (p<0.001).

Clinical conclusions
The authors concluded that patients receiving fluticasone propionate experienced a reduction in emergency department visits and hospitalisations.
Measure of benefits used in the economic analysis
No summary measure of benefit was used in the analysis. In effect, a cost-consequences analysis was performed.

Direct costs
The direct costs included in the analysis were the mean total asthma charges in the preindex period and the total costs (unadjusted and adjusted) for asthma care in the postindex period. No further details of the costs were provided. The authors stated that the data were provided from insurance claims records. The quantities and the costs were not reported separately. The authors did not report whether or not discounting was undertaken.

Statistical analysis of costs
Standard deviations were presented with CIs. A multiple linear regression analysis was conducted to compare the three groups in term of postindex asthma care charges. A logistic regression model was used to investigate the relationship between each drug group and hospitalisations and emergency department visits during the follow up period. The time to additional therapy for each group was determined using Kaplan-Meier survival analysis.

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

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out on sub-groups to determine whether the differences in overall asthma care charges were observed in the individual cohorts. The sub-groups were age 12 years and over and age 4 to 11 years. Kaplan-Meier survival analysis was also performed to determine the time to additional therapy among the three treatment groups.

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

Cost results
The preindex median charges were $90 for the fluticasone propionate group, $120 for the montelukast group and $118 for the zafirlukast group.

The preindex mean charges were $445 for the fluticasone propionate group, $355 for the montelukast group and $838 for the zafirlukast group.

Charges, both unadjusted and adjusted, were reported. The charges appear to have been adjusted, using a regression model, to account for highly skewed data, but details were not given.

With fluticasone propionate, the unadjusted total charge for asthma care in the postindex group was $576 (95% CI: 413 - 738) and the adjusted charge was $528 (95% CI: 508 - 547), for all ages.

For the group aged over 12 years, the unadjusted charge was $602 (95% CI: 421 - 791) and the adjusted charge was $536 (95% CI: 510 - 562).

For the 4- to 11-year-olds, the unadjusted charge was $426 (95% CI: 299 - 554) and the adjusted charge was $425 (95% CI: 386 - 463).
With montelukast, the unadjusted total charge for asthma care in the postindex group was $902 (95% CI: 689 - 1,116) and the adjusted charge was $967 (95% CI: 931-1,003), for all ages.

For the group aged over 12 years, the unadjusted charge was $893 (95% CI: 652 - 1,134) and the adjusted charge was $961 (95% CI: 916 - 1,007).

For the 4- to 11-year-olds, the unadjusted charge was $959 (95% CI: 550 - 1,369) and the adjusted charge was $932 (95% CI: 837 - 1,028).

With zafirlukast, the unadjusted total charge for asthma care in the postindex group was $1,417 (95% CI: 775 - 2,060) and the adjusted charge was $1,359 (95% CI: 1,300 - 1,419), for all ages.

For the group aged over 12 years, the unadjusted charge was $1,420 (95% CI: 764 - 2,076) and the adjusted charge was $1,391 (95% CI: 1,317 - 1,465).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
In asthma patients who had not been taking either an inhaled corticosteroid or leukotriene modifier, treatment with fluticasone propionate (a corticosteroid) was less costly than treatment with montelukast or zafirlukast (leukotriene modifiers). The use of fluticasone propionate resulted in less emergency department visits and less hospitalisations.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of comparator. The literature has often compared the corticosteroid fluticasone propionate with leukotriene modifiers, but its superiority in a clinical setting has not been identified.

Validity of estimate of measure of effectiveness
The basis of the analysis was a retrospective cohort study, which was appropriate for the study question. The study sample was representative of the study population. The patient groups were shown to be comparable at the baseline analysis.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was, in effect, a cost-consequences study.

Validity of estimate of costs
The authors did not present details of the costs used in the analysis, apart from stating that they were obtained from insurance claims records. Therefore, it is impossible to say whether all the categories of costs relevant to the perspective adopted were included in the analysis. The costs and the quantities were not reported separately and a statistical analysis of the quantities and prices was not performed.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and the issue of generalisability was addressed. The authors do not appear to have presented their results selectively. The study enrolled patients with a diagnosis of asthma who were aged older than 4 years, and this was reflected in the authors’ conclusions. The authors reported a number of further limitations to their study. First, montelukast was not available until the first quarter of 1998, therefore there was only a 9-month follow-up. This affects the extrapolation of resource...
use beyond the first 9 months. Second, the results may not be generalisable, as the data were obtained from claims data from managed care populations. Third, some patients might have been misclassified. Fourth, the sample was small and the small number of hospitalisations might explain why a statistically significant difference was not observed in asthma-related hospitalisations. Finally, unobserved variables were not considered and these could, potentially, be associated with the outcome.

**Implications of the study**
The authors recommended that the results be validated with a prospective randomised study.

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