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 study examined early intervention with low-dose budesonide (Pulmicort, Turbuhaler) in adult patients with mild persistent asthma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with mild persistent asthma. The patients were aged between 5 and 66 years of age.

Setting
The setting appears to have been primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from a clinical study published in 2003 (Pauwels et al., see 'Other Publications of Related Interest' below for bibliographic details). The resource use data appear to have been derived from the same clinical study but published elsewhere (see 'Other Publications of Related Interest' below for bibliographic details of these studies). The cost data were collected during 1995 to 2001. The price year was 1999.

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

Link between effectiveness and cost data
The resource data were collected using a different patient sample from that used in the effectiveness study.

Study sample
The authors stated that the study was not sufficiently powered to permit a sub-group analysis by country, although further information on the sample size calculations was not reported. Patients were considered for inclusion if they had mild persistent asthma, were aged between 5 and 66 years of age, were diagnosed less than 2 years ago, and had not undergone regular treatment with inhaled corticosteroids. No further details of the methods used to select the sample were provided. The total number of patients randomised to each of the study groups was also not reported, although the authors referred to two other studies in which details of the patients' characteristics and study methods were reported.
The trial included a total of 7,165 patients from 32 countries (i.e. 895 from the USA, 85 from Australia, 114 from Canada, 869 from China, 114 from France, 291 from Spain, 120 from Sweden and 39 from the UK). No reason was given for the differences in sample size per country. It was not reported whether some patients were excluded for any reason from the initial study sample.

**Study design**
The study was a 3-year RCT. The trial was multi-centred and multi-national. Patients from 32 countries were recruited. The randomisation method used to allocate the patients to the alternative treatment arms was not reported in this paper. A double-blind method for assessment of the outcomes was reported. The design of this trial was described in full elsewhere (Pauwels et al. 2003).

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. For patients who dropped out, effectiveness data were linearly extrapolated to the full 3-year study period. The two groups were shown to be comparable in demographic terms, clinical characteristics and drug use at baseline. No adjustment for confounding factors was reported. The main health outcome used in the analysis was asthma symptom-free days (SFDs), which was defined as a 24-hour period with no asthma symptoms. The authors also reported the reduction in hospital stay, emergency room visits and the hazard rate of severe asthma-related events (i.e. events requiring hospitalisation or emergency treatment due to worsening of asthma, or death due to asthma) for patients receiving budesonide, compared with those receiving placebo.

**Effectiveness results**
Compared with patients receiving only usual asthma therapy, the patients treated with budesonide experienced 14.1 more SFDs per year, (p<0.001), had 69% fewer hospital stays, (p<0.001), and 67% fewer emergency room visits, (p<0.05).

The reduction in the hazard rate of severe asthma-related events was 44% for patients receiving budesonide, (p<0.001).

**Clinical conclusions**
Early intervention with budesonide has been shown to be an effective therapy in patients with mild persistent asthma. It significantly improved SFDs and reduced hospitalisations, emergency visits and severe asthma-related events.

**Measure of benefits used in the economic analysis**
The benefit measure used was disease specific (i.e. asthma SFDs). This summary measure of health benefit was directly obtained from the effectiveness analysis. The benefits were discounted at a rate of 3%.

**Direct costs**
The direct costs reported were those of the health service. The health care resource use data were collected prospectively from the RCT. The key resource use categories included were medication, hospitalisation, emergency visits, physician visits, nurse visits and telephone contacts. International sources for resource and unit costs were appropriately referenced. The costing appears to have been based completely on actual data. The resource use and unit costs per country were not reported. The costs were discounted at a rate of 3%. Details of the analytical methods used were reported to have been presented in another study (Sullivan et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details).

**Statistical analysis of costs**
Since the authors showed the p-values obtained when comparing some of the costs estimated, statistical analyses of the costs were performed. The methods used were not reported in this paper.
Indirect Costs
Given that the trial population included both children and adults, lost work and school days were accounted for as productivity costs. The cost of a day's absence from work was calculated using the human capital approach, while absences from school were given the same value as absences from work. The costs were discounted at a rate of 3%.

Currency
Eight different local currencies were used in the analysis. These were US dollars ($), Australian dollars (Aus$), Canadian dollars (Can$), Chinese yuan (Y), French francs (Ffr), Spanish pesetas (Pts), Swedish kroner (SEK) and UK pounds sterling (£).

Sensitivity analysis
A probabilistic sensitivity analysis may have been performed since 95% confidence intervals were reported for the estimation of incremental cost-effectiveness ratios (ICERs). However, the authors did not report whether any sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section. Estimations of SFDs per country were not reported.

Cost results
The total cost estimates per country were not reported.

Synthesis of costs and benefits
ICERs were estimated as the extra cost incurred per additional SFD obtained with treatment with budesonide when compared with placebo. These ICERs were reported in local currencies. From the perspective of a health care payer, budesonide would be the dominant strategy in Australia (with an incremental cost -Aus$2.2 per additional SFD obtained). In Sweden, Canada, France, Spain, UK, China and the USA, the ICERs ranged from $2.4 to $11.3 per SFD. From a societal perspective, budesonide would be cost-saving in Australia, Canada and Sweden, while in the countries where an additional cost was required, the ICERs ranged from $0.1 to $9.2 per SFD.

Authors' conclusions
Early intervention with budesonide was shown to significantly improve the number of symptomatic-free days (SFDs) experienced by patients with mild persistent asthma.

CRD COMMENTARY - Selection of comparators
A placebo arm was used as the comparator. This approximated usual asthma therapy, as would be practised in the various participating countries (although no more details of these current practices were provided). You should decide whether this could be a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from an RCT. This was appropriate for the study question since this type of design is less subject to bias. The methods used to select the patients and to randomly allocate them to the study arms were not reported in this paper. Thus, it was not possible to assess whether the methods used were appropriate. The patient groups were shown to be comparable at analysis in terms of demographic and clinical characteristics, and drug use at baseline. An intention to treat analysis was performed, which is the optimal type of analysis to estimate the true benefit derived from the study intervention. Although not mentioned by the authors, the study sample is likely to have been representative of the study population on account of its relatively large size. The implications of using
effectiveness results from different countries should have been discussed further.

Validity of estimate of measure of benefit
The benefit measure used in the economic analysis was disease specific, thus making it difficult to compare with the benefits of other health care interventions. As the authors acknowledged, the use of quality-adjusted life-years would have enabled comparisons of the study results with those from other interventions.

Validity of estimate of costs
The authors explicitly identified the perspective adopted in the analysis. It seems that all the categories of cost relevant to the perspective adopted have been included. A statistical analysis of the costs was performed, although the authors did not report the methods used to obtain them. The authors emphasised that the incremental costs would vary with local unit costs and that care should be taken when extrapolating the results. The authors appear to have performed appropriate currency conversions. Discounting was performed.

Other issues
The results might have been probabilistic since 95% confidence intervals were reported for the ICERs, although this was not explicitly stated in the report. The ICERs were reported in local currencies, although it would have been more useful had they been reported in US$ purchasing power parity, in order to facilitate the comparison. The authors appropriately discussed the main limitations of their study. In particular, the fact that incremental benefits and resource use for the treatment of asthma might differ between countries.

Implications of the study
The authors remarked that, with the exception of cases of dominance, policy implications can only be judged locally on the basis of the health system's willingness to pay for an additional SFD. For countries where costs with budesonide are higher, the decision to implement this treatment would be determined by each health system's willingness to pay.

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Other publications of related interest


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