Cost-effectiveness of inhaled steroids in asthma: impact of effect on bone mineral density
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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 compared quick relievers (e.g. short-acting beta-antagonists) on an as-needed basis with the combination of a quick reliever plus inhaled corticosteroids (ICS) in the treatment of patients with mild-to-moderate persistent asthma. The dose of ICS was 200 microg twice per day (400 microg once per day). Further details of the quick relievers were not reported.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The population comprised a hypothetical cohort of 10,000 35-year-old women with mild-to-moderate persistent asthma.

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

Dates to which data relate
The effectiveness data were derived from studies published between 1988 and 2001. The costs were obtained from the parent economic evaluation (Paltiel et al. 2001) and from a study published in 2000. The price year was 2003.

Source of effectiveness data
The clinical parameters used in the model were the femoral neck and trochanteric hip fracture rate, the total hip fracture rate due to age-dependent decline in BMD, and the effectiveness of ICS on BMD.

Modelling
A Markov chain state-transition simulation model was used to model the natural history of asthma. The purpose of the model was to estimate the benefits and costs for a cohort of patients over a 10-year planning horizon. The model was based on one developed by Paltiel et al. (2001, see 'Other Publication of Related Interest' below for bibliographic details). The health states, cycle length and time-dependent transition probabilities were not reported in the current paper (see Paltiel et al. 2001 for further details).

Sources searched to identify primary studies
The effect of ICS on BMD was derived from a systematic review that included 6 randomised controlled trials and 3
longitudinal studies. Age-dependent decline in BMD was obtained from large population-based studies. The design of these studies was not clear.

Methods used to judge relevance and validity, and for extracting data
The authors reported that a systematic review of the literature was conducted for the main effectiveness estimate (effect of ICS on BMD). The methods of the review were not provided, although study designs were stated. Femoral neck and trochanteric hip fracture rates were calculated using formulae developed and reported in published studies. The overall incidence of fractures for the model was calculated using the percentage of hip fractures relative to all fractures.

Measure of benefits used in the economic analysis
The measure of benefit used was the quality-adjusted life-years (QALYs). Preference weights for health states and health-related quality of life (HRQOL) were obtained from published studies (Moy et al. 2004 and Tosteson et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details). Although the benefits appear to have been discounted, the discount rate was not reported.

Direct costs
Health service costs were included in the analysis. These covered acute and chronic asthma care, fracture related-costs (including monthly nursing home costs), acute hospitalisation related to hip and other fractures, and medication. Details of the cost analysis were not reported in the current study; the reader is referred to the parent economic evaluation (Paltiel et al. 2001). The unit costs and the resource quantities were not analysed separately. The costs were estimated from published studies using the model to derive expected resource use in the case of emergency visits, urgent care visits and hospitalisations. The price year was 2003 and the costs were adjusted using the medical care component of the US Consumer Price Index. Although the costs were discounted, the discount rate was not reported in the current study. The study did not state whether the costs were average or marginal.

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

Indirect Costs
Productivity costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Parameter uncertainty was explored using one-way sensitivity analyses. The focus was those parameters which were directly associated with the effect of ICS on BMD. The ranges over which variables were tested and the methods used to derive them were not reported. The parameters investigated were ICS dose, effect of ICS on BMD, baseline level of bone health in the population, length of therapy, and linear versus decay effect of ICS on BMD. The authors also explored a scenario in which a linear continuous effect of ICS on BMD over time was assumed (i.e. duration of therapy of 10, 20 and 30 years and a lifetime effect). As the literature suggested the possibility of a non-linear relationship, two different non-linear models of the effect of ICS on BMD were also explored. It was assumed that the effect of ICS on BMD decreased exponentially over 10- and 20-year periods.

Estimated benefits used in the economic analysis
Over a 10-year time horizon, quick relievers resulted in an average of 7.32 discounted QALYs per patient while the
combination of ICS and quick relievers generated, on average, 7.58 discounted QALYs per patient.

No side-effects were considered in the baseline analysis. The results for the 30-year scenario and lifetime effect were presented in full.

**Cost results**
The strategy of quick relievers plus ICS therapy cost $12,988 discounted over 10 years.

The quick relievers alone strategy cost $6,396 discounted over 10 years.

The discount rate used was not reported. The results for the 30-year scenario and lifetime effect were presented in full.

**Synthesis of costs and benefits**
The incremental cost-utility ratio was $26,040 per QALY gained over a 10-year horizon of ICS compared with quick relievers alone.

The results for the 30-year scenario and lifetime effect were presented in full.

The incremental cost-effectiveness ratio was most sensitive to the effect of ICS on BMD, especially when patients reached 65 years of age and older, and to a continuous linear effect of ICS on BMD. It became less sensitive when a non-linear effect was assumed.

It was also reported that the results were most sensitive to variations in the dose of ICS. When the time horizon was extended to the lifetime of the cohort, the incremental cost-effectiveness ratio increased to $42,000 per QALY gained. In the case of using a high-dose of ICS (1,000 microg/day) over the patient’s lifetime and a high effect of ICS on BMD, the use of ICS was dominated by the use of quick relievers alone.

**Authors’ conclusions**
Inhaled corticosteroid (ICS) therapy offered good value for patients with mild-to-moderate asthma. However, the authors drew attention to the impact of high doses of ICS over prolonged periods.

**CRD COMMENTARY - Selection of comparators**
Despite recommendations that ICS should be the treatment prescribed, the first-line therapy in the authors’ setting appears to have been quick relievers. The comparison made seemed appropriate given the objective of the study.

**Validity of estimate of measure of effectiveness**
The authors reported that the source of the main effect parameter was a systematic review. However, the methods and conduct of the review were not reported. It would appear that the included studies were combined using weighted averages. The other parameters were derived from a number of published studies. No methods for the identification and selection of these studies and parameters were reported.

**Validity of estimate of measure of benefit**
The estimation of health benefits (QALYs) was modelled using a Markov model. The methods used to estimate the utility weights were not described as they were taken from published papers. Benefits were discounted although the discount rate was not reported.

**Validity of estimate of costs**
The authors did not explicitly state the perspective chosen in the cost analysis. However, as only direct medical costs were considered this gives some indication as to the limits of the perspective. The authors reported limited information on their cost analysis. The unit costs were partially reported, whereas the resource use quantities and sources were not;
this may limit the possibility of replicating the analysis in other settings. The price year was reported although the discount rate was not. No statistical analysis of the quantities or prices was undertaken, and this will hinder the interpretation of the findings.

**Other issues**
The authors made some comparisons of their findings with those from other studies, providing a balanced discussion the differences detected. The issue of the generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively. The study considered only female patients with mild-to-moderate asthma, a choice which was well justified by the authors. The authors reported a number of limitations to their study. First, there were problems with the availability of data around the efficacy of ICS therapy, the impact on bone health and HRQOL weights. Second, the impact of using oral corticosteroids on the risk of asthma exacerbations was not accounted for in the analysis. Third, the relationship between ICS and hip fracture was only indirectly and, hence, partially assessed by combining the effect of ICS on BMD and the association between BMD and hip fracture.

**Implications of the study**
The authors made no explicit recommendations for changes in policy or practice, nor did they provide recommendations for further research. However, the discussion highlighted areas where more research-based information is needed.

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**Bibliographic details**

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**Other publications of related interest**
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by NLM
MeSH
Administration, Inhalation; Adrenal Cortex Hormones /adverse effects /economics /therapeutic use; Aged; Asthma /diagnosis /drug therapy /mortality; Bone Density /drug effects; Cost-Benefit Analysis; Female; Hip Fractures; Humans; Markov Chains; Middle Aged; Models, Theoretical; Quality-Adjusted Life Years; Treatment Outcome

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