Cost-effectiveness analysis of omalizumab in adults and adolescents with moderate-to-severe allergic asthma

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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 use of omalizumab, a recombinant humanised monoclonal anti-IgE antibody, in adults and adolescents with moderate-to-severe allergic asthma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults and adolescents with moderate-to-severe allergic asthma. The patients had to be symptomatic despite treatment with inhaled corticosteroids, and had to have positive immediate skin prick test responses to more than one common allergen (mites, cockroach, dog and cat). They were also required to have total serum IgE levels of greater than 30 to less than 700 IU/mL, and to have forced expiratory volume in 1 second (FEV1) values of greater than 40% to less than 80% of predicted values. Patients taking other asthma controller drugs and current smokers were excluded.

Setting
The setting was primary care. The economic study was conducted at the University of Missouri-Kansas City School of Medicine, USA.

Dates to which data relate
The effectiveness data were derived from two studies published in 2001. The resource use data were derived from the same studies as those used for the effectiveness data, and from author assumptions. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from two published studies.

Link between effectiveness and cost data
The resource use data were collected retrospectively from the two studies that provided the clinical effectiveness evidence.

Outcomes assessed in the review
The outcomes assessed were:
the number of successfully controlled days (SCDs);

the proportion of patients with an increase of 0.5 points or more in the Juniper Asthma Quality of Life Questionnaire (AQLQ; see Measure of Benefits Used in the Economic Analysis) score from baseline values, considered a measure of treatment success;

the incidence of adverse events; and

the length of hospital stay (LOS).

The authors reported that the LOS in hospital could not be obtained from the included studies.

**Study designs and other criteria for inclusion in the review**
The two included studies were multi-centre, randomised, double-blind, placebo-controlled Phase 3 clinical trials conducted in adolescents (aged 12 or older) and adults. Studies were excluded if they had a paediatric population, intravenous administration of omalizumab, or lacked sufficient data. One additional study was used, but its design was not reported.

**Sources searched to identify primary studies**
MEDLINE and EMBASE were searched for primary studies.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Two studies were included in the review (Busse et al. and Soler et al., see Other Publications of Related Interest).

**Methods of combining primary studies**
The two studies included in the review were pooled. Patients taking asthma controller drugs other than inhaled corticosteroids were excluded, as were current smokers. The method used to pool the studies was not reported. A total of 1,071 patients were included in the analysis, of whom 542 (245 men) were randomised to omalizumab and 529 (238 men) to placebo. The mean age was 39.7 years in the omalizumab group and 39 years in the placebo group.

**Investigation of differences between primary studies**
The authors reported that both studies used an identical protocol, with both studies using the same study design and having similar study populations.

**Results of the review**
The authors did not report the results of the review in terms of the number of SCDs and the AQLQ scores.

The incidence of adverse events was reported not to be statistically significant (the results were not shown).

On the basis of a published study, the average LOS was 3.8 days.
No specific measure of benefits was used in the economic analysis. The authors derived the measure of benefits from the effectiveness results. The measures of benefits used were the number of SCDs and the proportion of patients with an increase of at least 0.5 points in the AQLQ score from baseline values. The AQLQ is grouped into 4 domains corresponding to activity limitations, emotions, symptoms, and exposure to environmental stimuli. Each question is answered by patients on a 7-point scale according to level of impairment, with a lower score reflecting greater impairment. An SCD was defined as a day on which all of the following were met: morning peak expiratory flow rate of 90% or greater of baseline value, daytime score of 1 or less, night-time asthma score of 0, and rescue medication use of 2 puffs or fewer.

Direct costs
The resource use and costs were reported separately. The direct costs included in the analysis were those to the third-party payer. These were for omalizumab, rescue medication (albuterol), treatment for drug-related adverse events, unscheduled physician visits, emergency department visits and hospitalisations. The resource use data were derived from the two studies and from authors' assumptions. The authors assumed that 25% of the study population randomised to the omalizumab group received 225 mg twice monthly, while 75% received 300 mg monthly. The wholesale acquisition cost was used for omalizumab, and the average wholesale price for other medications. The average costs for an emergency department visit and an asthma hospitalisation were calculated on the basis of a published study. The cost of a physician visit was based on average reimbursements. The cost of oral steroids was not included in the analysis because of the very low cost of oral prednisone. The costs of adverse events were also not included.

Discounting was not relevant, as the follow-up period in both studies was one year, and hence was not performed. The study reported the average costs. All the costs were reported in 2003 dollars and were adjusted, when necessary, using the medical care component of the Consumer Price Index.

Statistical analysis of costs
The cost data were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis for successful treatment was performed by calculating the costs to achieve a 1.5 point increase, as well as a 0.5 point increase, in the AQLQ score. A sensitivity analysis was also performed using the best- and worst-case scenarios. The lowest acquisition and hospitalisation cost for the omalizumab group, and the highest hospitalisation cost for the placebo group, were used for the best-case scenario. The highest acquisition cost of omalizumab was used for the worst-case scenario. The Federal Supply Schedule cost of omalizumab was also used for the sensitivity analysis.

Estimated benefits used in the economic analysis
The authors did not report the estimated benefits used in the economic analysis.

Cost results
The mean daily asthma treatment costs were $39.85 per patient for patients treated with omalizumab compared with $2.08 per patient for those treated with placebo.
Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio (ICER; i.e. the additional cost per incremental SCD with omalizumab). The ICER was $523, indicating that it costs an extra $523 per day for an additional SCD with omalizumab. The mean daily cost of treatment for each patient achieving at least a 0.5-point increase in the AQLQ score was $378.

The results from the sensitivity analysis revealed that the daily costs of achieving a meaningful improvement in the AQLQ score ranged from $81 to $2,626. The daily costs to achieve an additional SCD ranged from $148 to $1,273.

Authors' conclusions
Omalizumab was clearly more expensive than other controller medications and had modest efficacy in patients with moderate allergic asthma.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. A placebo was used in the two clinical trials that provided the clinical evidence. Omalizumab was not compared with inhaled corticosteroids, which are alternative treatments for asthma. You should decide whether placebo is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
Although MEDLINE and EMBASE were searched, it was unclear whether a systematic review of the literature had been undertaken to identify relevant research and minimise biases. However, the authors reported the methods and conduct of the review satisfactorily. The effectiveness data were derived from two randomised controlled trials, which are considered the 'gold' standard when comparing different health interventions. The authors also reported that both studies had identical protocols and study populations. The effectiveness estimates were combined, although the authors did not report the method used. The authors showed that there were no differences in baseline characteristics in the two pooled study groups.

Validity of estimate of measure of benefit
The estimation of benefits was derived from the meta-analysis, the results of which were not reported. This will hamper the generalisability of the authors' results, as well as the internal validity of the study.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. However, some relevant costs were omitted from the analysis. The authors reported that the costs of oral steroids were not included because of the very low cost of oral prednisone, but these omissions were unlikely to have affected the authors' conclusions. The costs of adverse events were not included since the incidence of severe anaphylactic reactions was low, the incidence of adverse events was not statistically significant, and there was a lack of clear evidence that omalizumab could increase the evidence of malignancies.

The costs and the quantities were reported separately, which will enhance the generalisability of the results to other settings. Resource use was derived from the two pooled studies, but the authors had to assume the average LOS based on another study and the proportion of patients receiving 225 mg or 30 mg omalizumab. The unit costs were derived from published sources. Appropriate sensitivity analyses of the costs were performed by considering best- and worse-case scenarios. Discounting was not relevant, as all the costs were incurred during one year, and was not performed. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors reported that this was the first cost-effectiveness analysis of omalizumab. However, they compared their results with studies that compared the use of other controller medications and reported lower incremental costs per
symptom-free day than those for omalizumab. The issue of generalisability to other settings was partially addressed through the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of limitations to their study. First, one of the included studies was performed primarily outside of the USA. Hence, there might be differences (e.g. accessibility of medical care, need for medical treatment, or mode of asthma treatment) that could affect the results. However, as both studies used identical protocols, and both found similar event rates, it is likely that these differences were minimal. Second, the authors could not calculate the cost per quality-adjusted life-year gained (QALY) because the AQLQ score could not be transformed to the 0 to 1 scale necessary to construct a QALY gained, and little information on chronic side effects of omalizumab was available.

**Implications of the study**
Although omalizumab was found to be clearly more expensive than other controller medications in patients with moderate allergic asthma, the authors reported that omalizumab could be cost-saving if it was used on a very restricted group of patients with severe asthma.

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None stated.

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**Other publications of related interest**


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