Cost effectiveness of sublingual immunotherapy in children with allergic rhinitis and asthma


**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 the use of sublingual immunotherapy (SLIT) performed with high-dose allergen extracts (Staloral), compared with conventional treatment, pre-SLIT, for children with allergic rhinitis and asthma.

**Type of intervention**
Treatment.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
The population comprised children under the age of 18 years with allergic disease (perennial or seasonal), that is, allergic rhinitis and/or allergic asthma. The allergic asthma sub-population was examined separately in a secondary analysis.

**Setting**
The setting was specialist outpatient care at one allergy centre, located in the north of Milan. The economic study was carried out in Italy.

**Dates to which data relate**
The date range for the chart review was not reported. The price data were taken from sources published between 1996 and 2003. No price year was reported.

**Link between effectiveness and cost data**
In the main analysis, the costing was undertaken on the same sample of patients as the effectiveness analysis, using the same approach of retrospective patient chart review. In the asthma sub-group analysis, the costs were again based on the same patient records as the effectiveness analysis, although the databases from which the records were drawn differed (see Study Design).

**Study sample**
A total of 135 patient records were extracted. Of these, 46 patients had perennial allergy and 89 had seasonal allergy, with comparable age and gender distribution. The mean age was 12.10 years (standard deviation, SD=3.63; median 11.00) at database extraction and 7.37 years (SD=3.63; median 6.73) at SLIT initiation. Grass pollen was the most frequent allergen type (52.6%), followed by house dust mites (34.1%). The most frequent clinical diagnosis at database inclusion was a combination of rhinitis and asthma (44.4%), followed by asthma alone (30.4%).
The asthma sub-group had 41 patients treated with SLIT and 35 control patients. Age at SLIT initiation was comparable with the age at database extraction in the control group (see 'Study Design').

**Study design**
A within-group comparison using patient chart review was performed at a single study centre. Patients were included only if data were available for the full follow-up period (4 years), that is, 1 year of data prior to receiving SLIT and 3 years of data on SLIT. Demographic data, outcome measures and resource consumption measures were tabulated. To facilitate a meaningful cost comparison, a second case-control analysis was undertaken. This involved a sub-group of patients (from the original patient selection) with allergic asthma and a control group of patients with identical characteristics but not treated with SLIT, extracted from a network database of paediatricians in the same area (Pedianet).

**Analysis of effectiveness**
The outcome measures included the number of rhinitis and asthma exacerbations, specialist visits and absences from nursery or school. Nursery or school days lost were used as a proxy for the number of working days lost by parents. Hospitalisations were not retrievable from the main dataset, although they were available in the dataset for the asthma control group.

**Effectiveness results**
The results were consistent for both the whole population and the perennial and seasonal sub-samples:
- the mean number of exacerbations was about 5 times lower during the SLIT period (reduced from 45.0 to 6.9 per patient/year in the whole population);
- the mean number of medical visits was about 3 times lower (reduced from 9.9 to 2.3 per patient/year in the whole population); and
- the mean number of nursery or school days lost was about 4 times lower (reduced from 37.9 days to 7.3 days per patient/year in the whole population).

In the asthma sub-group, outcome measures also declined considerably during SLIT for SLIT-treated patients:
- mean exacerbations decreased from 46.1 to 7.2 per patient/year;
- mean medical visits decreased from 9.6 to 2.5 per patient/year; and
- mean nursery or school days lost decreased from 37.5 to 7.2 per patient/year.

**Clinical conclusions**
A substantial reduction was found in all outcome measures during the SLIT period compared with the pre-SLIT period.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of benefit. Therefore, a cost-consequences analysis was performed.

**Direct costs**
The direct costs examined in the main analysis included drugs for allergic disease, specialist visits and SLIT. Prices were retrieved from declared national published sources dating from 1996 to 2003. Hospitalisation costs were not included in the analyses because data were not available for the SLIT-treated patients and were only available for the asthma control group in the sub-analysis. The average cost per patient was calculated over a total follow-up of 4 years (1 year before SLIT and 3 years during SLIT) for SLIT-treated patients and for 4 years' conventional treatment in non
SLIT-treated patients.

**Statistical analysis of costs**
Mean costs, SDs and median costs were reported.

**Indirect Costs**
The indirect costs examined in the main analysis included those arising from child schooling lost and parental work loss. The value of days lost was determined according to published methodology and income measures. Indirect costs were not included in the asthma sub-analysis because of a lack of data in the control group database. The price year was 2002.

**Currency**
Euro (EUR).

**Sensitivity analysis**
Uncertainty and data variability were not investigated.

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

**Cost results**
The average annual cost/patient was EUR 2,672 before SLIT initiation and EUR 629 during SLIT.

Similar results were found for perennial and seasonal allergen sub-groups.

The asthma sub-analysis showed a total cost over 4 years’ follow-up of EUR 1,182 for SLIT patients and EUR 1,100 for controls.

**Synthesis of costs and benefits**
No synthesis was performed.

**Authors’ conclusions**
High-dose sublingual immunotherapy (SLIT) may be effective in reducing both the clinical and cost burden of allergic rhinitis and asthma in children with allergic disease over 4 years’ follow-up. The authors believed that the study was likely to represent an underestimation of the true effect of SLIT on costs, because reductions in hospitalisations might also be expected.

**CRD COMMENTARY - Selection of comparators**
The comparator was standard or conventional treatment for allergic disease. Although the authors stated that immunotherapy is the only treatment acting on the cause and not the symptoms of disease, it was unclear to what extent conventional treatment comprised subcutaneous immunotherapy and/or other modes of administering immunotherapy and/or other therapies. The confusion was increased by the fact that the authors stated that SLIT was introduced primarily for “safety reasons”, that is, efficacy differences between routes of administration were not expected. The authors did not discuss whether conventional treatment might have differed between the periods before and after SLIT was introduced and whether this should be accounted for in the analyses. You should decide whether the comparator is relevant to your own treatment setting.
Validity of estimate of measure of effectiveness
The main analysis was based on a within-group comparison, which the authors acknowledged was an inferior design in terms of the study question (the effectiveness of SLIT). However, they stated that the present analysis was performed as a precursor to prospective, observational work and was intended only to provide an initial estimate. The reader should bear this caveat in mind if intending to rely on the results. It was not established in the publication whether the study sample was representative of the study population, given the use of only one study centre and the inclusion criterion of adequate follow-up data for 4 years. Patient characteristics were reported, allowing the reader to make their own judgement. The retrospective and within-group nature of the study represents a limitation to its internal validity. No power calculations were reported and no statistical testing of the results was performed. This makes it impossible to ascertain whether the results obtained were in fact due to SLIT.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed. The reader should refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective was societal and both direct and indirect costs were analysed in the main within-group comparison. Some relevant costs (i.e. diagnostic tests, hospitalisations, adverse events and concomitant medications) were excluded from all analyses. Indirect costs were excluded from the second case-control asthma analysis. These omissions make it difficult to be confident in the cost estimates obtained, although the authors noted their belief that the cost-effectiveness of SLIT was underestimated because of the non-inclusion of hospitalisations. Resource use was taken from the same data source as effectiveness measures, while prices were taken from national published sources. No price adjustments or discounting were applied, although prices for different resource types were drawn from different years and costs during SLIT were calculated over a 3-year period. Unit cost sources, but not values, were reported. As the authors implied that this analysis was a precursor to a more robust prospective study, the level of costing undertaken is likely to be adequate and fit for this purpose.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and found them, generally, to be in agreement. The authors did not address the issues of generalisability or potential variability in the data. The results were not presented selectively. The authors' conclusions reflected the scope of the analysis.

The authors acknowledged several limitations of their study. First, the incomplete cost data, which did not include diagnostic tests or hospitalisations (the latter known to be common and expensive). Second, the short-term nature of the study (only 3 years of SLIT and no post-SLIT follow-up). Third, the fact that the second case-control analysis was not conducted on the full patient population as originally selected, partly because of the difficulty in finding a control group with sufficient retrospective data.

Implications of the study
The authors suggest that further studies, using a prospective observational design, should be conducted to validate these results.

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None stated.

Bibliographic details

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Subject indexing assigned by NLM