

ORIGINAL ARTICLE

A cost-effectiveness analysis
of immunotherapy with SQ
allergen extract for patients
with seasonal allergic
rhinoconjunctivitis in selected
European countries

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Key words: Cost-effectiveness – Immunization therapy – Rhinoconjunctivitis

ABSTRACT

Background: Seasonal allergic rhinoconjunctivitis can, for some people, reduce quality of life and the ability to cope with everyday tasks.

Scope: In this paper we investigate the cost-effectiveness of immunization therapy with Alutard SQ (ASQ) and compare the cost-effectiveness in countries where the therapy has been in use in order to assess the impact of national therapeutic practices on the results of health economic assessments. Data are obtained from a clinical trial carried out in 2001–2002. To evaluate the cost-effectiveness of immunization we have added data on resource use in Austria, Denmark, Finland, Germany, the Netherlands, and Sweden.

Findings: The computations result in cost-effectiveness ratios for allergen immunization

between €10 000 and €20 000 per QALY even without provision for indirect costs, and achieving dominance in most countries where indirect costs have also been taken into account. The country comparisons show that the direct cost of administering the up-dosing and maintenance differs considerably between countries, and that the cost of medical staff is substantial, constituting in most cases more than half of the direct costs of the immunization therapy.

Conclusion: The study shows that immunotherapy with SQ allergen extract is cost-effective in a wide range of national environments, and that cost-effectiveness differences by country are largely a result of different practices in the up-dosing phase.

Introduction

Seasonal allergic rhinoconjunctivitis (SAR) is, in some cases, an uncomplicated condition that can be controlled by conventional pharmacotherapy and by avoiding allergens. However, for some people, either this is not enough to control the symptoms, or the drugs used may have undesired side-effects. For these people, the condition results in a severe reduction of quality of life and, in addition, it represents a social problem, for

example in the case of young people attending school. Severe SAR results in a reduced ability to cope with everyday tasks – at work or school – and it may also affect other aspects of health¹.

The present paper has a double purpose: first of all, we are reporting on a clinical trial of a specific allergen immunotherapy which has already been in use for many years. Second, the results of the clinical trial are then used to derive cost-effectiveness ratios with respect to several types of outcomes (days without symptoms,

quality of life). This health economic assessment has been carried out for several countries in which the therapy is currently used, and the assessment of the cost of the therapy has been based on the actual resource use of each country, as well as on the relevant prices. This makes it possible to compare cost-effectiveness in different countries and thereby obtain a practical perspective on the viewpoint, repeatedly put forward in the discussion of how to conduct health economic evaluations, that assessments of cost-effectiveness of medical interventions are strongly dependent on the country in which they are carried out. This means that results obtained in one country cannot meaningfully be applied to other countries, even between countries which are similar with respect to economic structure as well as therapeutic tradition. In addition, the present intervention, which is not new and has already been adopted for some years in the countries investigated, provides an unusual opportunity for making such comparisons. This is because it is possible to use data from actual therapeutic practice, a possibility which is not available when the intervention studied is so new that data on resource use can only be obtained from clinical studies.

As will emerge from the study, the results obtained for the countries covered by the analysis, namely Austria, Denmark, Finland, Germany, the Netherlands and Sweden, are considerable. In all these countries, the treatment by immunotherapy is shown to be a reasonably advantageous intervention when only direct costs are considered, as measured by the standards of magnitudes of cost-effectiveness ratios which are increasingly becoming generally accepted. If the effects on the number of workdays delivered are also taken into consideration, then treatment by immunotherapy is shown to be very advantageous, since in this case, society not only gains a more healthy population, but also saves money due to productivity increases, which in most countries offset the cost of the therapy. Within this general framework, countries do display big differences, which will be considered in detail at the end of the paper.

Alutard SQ* (ASQ) is an allergen immunotherapy aimed primarily at people experiencing moderate-to-severe SAR. ASQ has a fast symptom relief with a significant decrease in SAR symptoms, and will lead to a significant reduction in the need for other medications². The treatment significantly improves quality of life ($p < 0.01$)³. ASQ immunotherapy has been shown to have a persistent and similar effect for up to 9 years after termination of treatment, regardless of whether the allergen was tree pollen, grass pollen, animal hair, or venom (Jacobsen *et al.* (9 years), Mosbech *et al.*⁵

(9 years), Durham *et al.*⁶ (7 years), Hedlin *et al.*⁷). ASQ thus covers a broader spectrum of therapies.

As well as its effect on rhinoconjunctivitis, ASQ has been shown to reduce the risk of developing asthma later in life⁸. This has important consequences, as approximately 20% (rising to 40%) of all rhinoconjunctivitis patients develop asthma at a later^{9,10} stage. Asthma is not only a disease which seriously reduces the quality of life, it is also one which constitutes a considerable drain on a country's resources, both in the healthcare sector and on society in general. According to Berggren *et al.*¹¹, severe asthmatics used 2–5 times more resources in healthcare than the general population. In the present analysis, which is based on clinical data on the everyday aspects of rhinoconjunctivitis rather than on their long-term implications, we have chosen not to take the reduction of risk of developing asthma into account since this information was not gathered in the UK Immunotherapy Study Group (UKIS) trial.

Immunisation with ASQ is administered by subcutaneous injections into the arm. The specific allergy vaccination involves an initial immunisation phase (up-dosing) and a maintenance phase. In the initial phase, the patients are given one or two injections weekly. The interval between the two injections is 30 minutes. During the initial immunisation phase, the dose is gradually increased to establish a maintenance dose or a maximum tolerated dose of ASQ. In the UKIS clinical trial, the initial phase included approximately seven visits to the allergy specialist. In actual practice – which may differ from country to country – the initial phase has duration of 11–15 weeks.

The maintenance dose is administered by one injection at each allergy clinic visit, and the interval between the visits is approximately 6 weeks, with a variation of ± 2 weeks, depending on the individual country's therapeutic practices.

The immunotherapy lasts for 3 years. After 3 years, it is assumed that the patient is immunised for an additional 6 years. Our assumption is based on long-term studies of subcutaneous immunotherapy (WHO¹², Durham *et al.*⁶, Mosbech *et al.*⁵, Walker *et al.*³), so that projection over 9 years in the present study may be considered as justified by the published data from available clinical research.

Methodology: the clinical study

The present pharmacoeconomic analysis is based on a clinical study, the UKIS study, carried out in the period October 2001 to September 2002. In this study,

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patients had specific immunotherapy with ASQ and the subjects were characterised as having SAR and not responding adequately to anti-allergic drugs. The study is reported in Frew *et al.*¹³.

The UKIS study was a multi-centre, double-blind, randomised, parallel-group trial comparing ASQ and placebo. The study included a screening visit to assess subject eligibility, and a randomisation visit followed by an up-dosing and a maintenance period. During the up-dosing period of 7–8 weeks, 15 injections were given, reaching the maintenance level of 100 000 unit doses (the UKIS study also included treatment at a level of 10 000 units, but the present cost-effectiveness study concentrates on the first treatment, considered to be the most effective in practice). In the maintenance period, injections were given approximately every 6 weeks. Before and during the pollen season (15 weeks from May to August) subjects were supplied with free emergency medication. During this time, subjects were asked to record hay fever symptoms, any emergency medication taken, and peak expiratory flow. A visual analogue scale (VAS) for allergic symptoms was completed by the subjects every week to assess allergic symptoms.

Male and female subjects aged 18–60 years with a clinical history of grass pollen-induced SAR not adequately controlled by antihistamines and topical steroids and/or sodium cromoglycate, and a positive skin prick test for grass pollen were included.

The primary efficacy endpoints were a symptom score and a medication score. A daily symptom score was recorded by each subject: allergic symptoms were categorised as nose symptoms (runny nose, blocked nose, sneezing, itchy nose), eye symptoms (gritty feeling/red/itchy eyes, watery eyes), lung symptoms (cough, wheeze, tightness/dyspnoea, exercise-induced symptoms). Each symptom was scored from 0 (no symptoms) to 3 (severe symptoms). Emergency

medication use was detailed in the diary card, and it was assigned scores as follows:

Sodium cromoglycate ocular drops	1 per drop
Acrivastine 8 mg	2 per capsule
Fluticasone propionate nasal spray 50 µg/spray	2 per spray
Prednisolone 5 mg	2 per tablet
Salbutamol 100 µg/puff	1 per puff
Desloratadine 5 mg	4 per tablet
Cetirizine 10 mg	4 per tablet

Secondary endpoints were (1) a weekly subjective evaluation of severity: subjects were asked the question 'How has your hay fever been this week?' using a 10 cm VAS for allergic symptoms from 0 ('no symptoms') to 10 ('severe symptoms'), and (2) the Rhinoconjunctivitis Quality of Life questionnaire overall score which was summarised by treatment and visit. Table 1 summarises the patient characteristics and the main findings from the UKIS study. The differences in mean medication score and mean symptom score were both significant, cf. Frew *et al.*¹³.

The quality of life data provided by the clinical trial were obtained using the Juniper Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Here the subjects assign scores to 28 aspects of health, in the categories (1)–(3) activities, (4)–(6) sleep, (7)–(13) non-nose/eye symptoms, (14)–(16) practical problems, (17)–(20) nasal symptoms, (21)–(24) eye symptoms, (25)–(28) emotions. Each of these categories consists of several items, for example the category non-nose/eye symptoms has components (7) fatigue, (8) thirst, (9) reduced productivity, (10) tiredness, (11) poor concentration, (12) headache, (13) worn out. For each of the 28 items, there are 7 possible levels (from worst case 0 to best case 6). The items in each category are aggregated by simple averages, giving a profile of 7 real numbers between 0 and 6.

Table 1. Patient characteristics at the start of the study and main findings in the UKIS study¹³

	ASQ (n = 203)	Placebo (n = 103)
Age (years)	38.33	37.85
Systolic blood pressure (mmHg)	125.5	123.6
Diastolic blood pressure (mmHg)	78.2	78.0
Pulse rate (beats/min)	72.7	72.8
FEV ₁ (L)	3.999	3.487
PEFR (L/min)	534.3	544.0
Skin prick testing reactions with <i>Phleum pratense</i> (mm)	8.8	9.4
Mean daily medication score	3.63	6.17
Mean daily symptom score during peak season	4.70	6.88
Mean VAS for allergic symptoms	2.34	3.07

Source: UKIS study: Frew *et al.*¹³

Assessment of cost-effectiveness

Model

For the calculation of cost-effectiveness in each of the countries, a simple comparison is made between two treatments, namely ASQ on the one side and emergency medication on the other. The comparison is projected over 9 years, where in the ASQ treatment, the first year covers the up-dosing and maintenance phase and the two following years of maintenance have follow-up visits to the specialist, while in the remaining years the two treatments differ only in the extent of the emergency medication. In the comparison treatment, all years are alike, and all medication is emergency medication during the pollen season. For comparison of costs and effects, current costs are discounted at a rate of 3%. It should be noted that the usual pharmacotherapy for seasonal allergic rhinitis would also include prophylactic treatment commencing pre-seasonally and continuing throughout with topical nasal corticosteroid plus antihistamine plus eye-drops if needed.

To assess the cost-effectiveness of treatment with ASQ, we calculated *incremental cost-effectiveness ratios* (ICERs), as the ratio between the cost difference between ASQ treatment and standard treatment divided by the difference in effect, however measured, between the two treatments. The ICER is the standard measure used for comparison of the aspects of treatments, widely used in the literature.

Cost data

The data for direct costs of the treatment with ASQ are obtained by combining the resource use as found in the UKIS study with national price data. For the resource, comparable products available in the relevant national market have been chosen. However, it must be taken

into account that there may be national differences in the resource use.

There are two distinct reasons for such national differences: one is to do with national practice associated with immunisation, where some countries use procedures other than those prescribed by the UKIS study, and in such cases we have employed actual resource use rather than that of the trial. The other reason for differences between countries stems from variations in the type of emergency medicine available, which may not always correspond with that of the trial, in which case we have used the one which is closest. The cost arising from loss of working days when obtaining immunotherapy injections has not been included, since data were not available in all countries, and the loss may be considered as being important to the results obtained.

To assess the indirect cost, which in this case consists of a productivity gain obtained through a reduced number of working days lost (information not provided by the UKIS study), we have used an estimate of the number of working days lost given in a Danish investigation of rhinoconjunctivitis patients¹⁴, which is 0.6 days for the ASQ treatment and 2.7 days for standard care. The indirect cost can then be calculated on a national scale by multiplying by the daily wage rate of the countries. The productivity loss arising from patients' visits to the doctor can be regarded as small and has not been included in the analysis.

The findings are presented in Table 2, where we have shown the difference in cost per patient in terms of net present value of cost differences over the 9 years. The comparison has been projected over 9 years in accordance with data from Mosbech *et al.*⁵ showing 6.5 years of effect after 2 years of treatment, while in the present model we have a 3-year treatment period.

As shown in Table 2, the cost differs considerably among countries; the main source of cost differences is the variation in therapeutic practices, whereas the variation in the cost of the medicine is much

Table 2. Incremental cost per patient of specific allergy vaccination (SAV) treatment with ASQ. Present value at 3% discounting, € (exchange rates as of September 2005)

	Austria	Denmark	Finland	Germany	Netherlands	Sweden
Up-dosing visits	116	858	388	108	649	701
Maintenance visits	203	543	1254	209	1133	2416
ASQ	1255	1115	959	1259	1470	781
Specific immunotherapy	1574	2516	2601	1575	3252	3898
Rescue medication	-101	-201	-44	-107	-79	-98
Other direct cost	-307	-39	-916	-232	-230	-1079
Direct cost	1166	2276	1642	1236	2942	2721
Indirect cost	-1294	-3600	-1958	-1774	-2168	-2118
Total cost	-129	-1324	-317	-538	775	603

Source: Muusmann¹⁵

smaller. For Sweden and Finland, the low cost of ASQ medication is a result of the changes in the exchange rates of these countries in later years and the price having been kept fixed by the authority in the local currency. Countries with several follow-up visits tend to display greater cost of immunisation.

For the indirect costs, which as mentioned above are found as the productivity gain assessed using country-specific daily wage rates, it is seen that they differ substantially between countries, with the Danish productivity gain being particularly large. It should be taken into consideration that national income tax systems and the financing of social security influence the daily wage rates, so that a lot of caution should be taken when comparing across countries.

It may be noticed that, although there are considerable cost differences, some of these offset each other, so that the figures for direct as well as indirect cost tend to vary less than their individual components. It is noticeable that there are large differences in the cost of treatment, more than in the cost of the medicine, which is fairly constant (the low figure for Sweden being attributable to the movements in the exchange rate). Also, the price of emergency medicine shows considerable variation. As a whole, the intervention gives rise to a net cost to society only as long as the direct cost of treating the patient is included. Adding indirect costs will change the picture, since the loss of working days with the standard treatment exceeds that of ASQ treatment, indeed to such an extent that there is a net gain to society.

days as days where the patient had no eye, nose, or lung symptoms. This was combined with the data on emergency medication to define a well-day as a day with no emergency medication and where the maximum sum of nose and eye symptoms was 2 points, and the sum of the lung symptoms was 0. The proportions of symptom free days in the pollen season were estimated in the UKIS study as 31.2% for the ASQ treatment and 23.6% for symptomatic treatment, and the percentage of well-days were estimated as 36.6% and 28.2%, respectively. The results obtained are shown in Table 3. In accordance with standard practice, we have used the terminology 'dominance' for the cases where the intervention results in *both* a reduction in cost and an increase in effects. This is seen to be the case in most countries when the productivity gain is included in the analysis (technically, total cost includes both direct and indirect cost, and the latter is a cost *reduction* due to the productivity gain).

The results may be compared to those obtained for levocetirizine, where incremental cost (over no treatment) was €9.81 per month or €117.7 per year, whereas the incremental days with inability to perform daily activities was 0.81 per month or 9.7 days a year, giving a cost-effectiveness ratio of 12.1 (measured as euros per day; cost data from France¹⁶). It should, however, be taken into account that the well days or symptom free days represent a more satisfactory measure of quality of life than does the ability to perform daily activities.

Effects: well-days and symptom-free days

For the measurement of effects of treatment, the RQLQ scores have been used to define *symptom-free*

Quality-of-life measures

RQLQ gives detailed information about quality-of-life improvements in the treatment of patients suffering

Table 3. Cost-effectiveness of treatments and incremental cost-effectiveness (ICER) of ASQ versus standard care. Outcome measured as symptom free days or well days

		Austria	Denmark	Finland	Germany	Netherlands	Sweden
Direct cost per symptom free day (€/day)	ASQ	9	15	15	10	19	22
	Standard care	4	4	8	4	3	6
	ICER	26	50.1	39	29	68	61.9
Total cost per symptom free day (€/day)	ASQ	11	21	19	13	22	26
	Standard care	16	37	27	22	24	30
	ICER	Dominance	Dominance	Dominance	Dominance	18	13.8
Direct cost per well day (€/day)	ASQ	8	13	13	9	16	19
	Standard care	3	3	7	4	3	8
	ICER	24	36.4	35	27	61	16.9
Total cost per well day (€/day)	ASQ	10	18	16	11	19	21
	Standard care	13	31	23	18	20	25
	ICER	Dominance	Dominance	Dominance	Dominance	16	15.3

Source: Muusmann¹⁵

from rhinoconjunctivitis. The change in overall RQLQ score, which is calculated as the average of the 7 domain scores, is given in Table 4, which shows that the treatment with ASQ results in a smaller reduction in quality of life during the pollen season than does the standard treatment.

Although well-suited for measuring quality of life as related to rhinoconjunctivitis, the RQLQ is not immediately suited to a comparison with treatments of patients suffering from other diseases. For this, one would need a conversion of RQLQ scores into some more general health-state measure, presumably to QALYs. For such a conversion, the EuroQoL 5-dimension EQ-5D instrument appears to fit, being based on a questionnaire that to some extent contains similar dimensions to those of the RQLQ, namely (i) mobility, (ii) self-care, (iii) usual activities, (iv) pain/discomfort, and (v) anxiety/depression, to be evaluated at three levels. The EQ-5D is increasingly being chosen as the preferred instrument for quality of life evaluation in cost-effectiveness analysis (cf. e.g. NICE¹⁷).

In the conversion, the RQLQ scores were averaged within the category 'activities' (to be identified with 'usual activities' in the EQ-5D), the categories 'practical problems', 'nasal symptoms', 'sleep' and 'non-nose/eye symptoms' (to be identified with 'pain/discomfort' in EQ-5D), and the category 'emotions' (identified with 'anxiety/depression'). The three resulting scores were then converted from numbers between 0 and 6 to numbers between 0 and 3. For any possible scoring

in the two remaining EQ-5D categories, this gave a full profile of scores which may then be converted into a QALY index. For this, the table of QALY values corresponding to EQ-5D scorings constructed by Dolan¹⁸ was used for each of the countries except Denmark, for which national tables of QALY values (Pedersen *et al.*¹⁹) were used.

The conversion method introduces two sources of indeterminacy in the assessment of incremental quality of life. First of all, it depends on the converting of RQLQ scores to EQ-5D scores, and secondly, the QALY values assigned to EQ-5D scores depend on the unknown scoring in the categories 'mobility' and 'self-care'. However, calculations performed using several alternative hypotheses show that the final results do not display great variation. Concerning the second problem, it seems furthermore reasonable to assume that the relevant patients have no problems with mobility and self-care. A similar approach, where a specific quality-of-life measure has been mapped to QALY values, is reported in Brown *et al.*²⁰, see also Meltzer²¹.

In calculating the QALY loss with or without treatment it should also be taken into account that this loss is restricted to a small part of the year, namely the pollen season which in the UKIS study was defined as 1st June to 13th August. The resulting net gains from the ASQ treatment as compared to standard treatment can be seen in Table 5. It may be noticed that the effects are lower for Denmark than for the other countries, a circumstance associated with the use of different tables for the transferral of EQ-5D scores to QALYs. In principle, the use of country-specific conversion tables should be considered preferable when reflecting the possible differences in utility of health states; it does however point to the somewhat imprecise nature of QALY assessments in general. If the same effect score is used for Denmark as for the other countries, the cost-effectiveness ratio changes to €19 667/QALY.

For the assessment of the magnitudes involved in the cases where the final result is not dominance (cost saving

Table 4. Change in overall RQLQ score during pollen season. Percentage of patients

Change from baseline to seasonal visit	< -0.5 (improvement)	-0.5 to 0.5	> 0.5 (deterioration)
ASQ	5.5	21.3	73.2
Symptomatic medication	2.2	8.7	89.1

Source: UKIS: Frew *et al.*¹³

Note: Seasonal visits between 6 June and 30 June

Table 5. Incremental cost, effects, and cost-effectiveness ratios of treatment with ASQ compared to standard treatment

	Austria	Denmark	Finland	Germany	Netherlands	Sweden
Direct cost (€)	1166	2276	1642	1236	2942	2721
Total cost (€)	-129	-1324	-317	-538	775	603
Effects (QALY)	0.12	0.088	0.12	0.12	0.12	0.12
Cost-effectiveness ratio, direct cost only (€/QALY)	9716	25 863	13 683	10 300	24 517	22 675
Cost-effectiveness ratio, all cost included (€/QALY)	Dominance	Dominance	Dominance	Dominance	6458	5024

Source: Muusmann¹⁵

as well as better effect), one may compare with the rules-of-thumb in use in most countries, recently made explicit by NICE (NICE¹⁷, p.33), according to which interventions which cost up to £20 000 (€29 184) may be considered as using society's resources in an effective way. According to this viewpoint, the ASQ treatment is cost-effective even without taking productivity gain into consideration.

Discussion

In the preceding sections, we have described the data and method of calculation, and the main results have been presented. To assess the robustness of the results, sensitivity analyses have been carried out on the number of up-dosing visits, cost of immunotherapy visit, cost of GP and/or specialist visit, cost of emergency medicine, and effectiveness of the immunotherapy. Only very considerable changes in the base values will turn the cost-effectiveness ratios into unfavourable ones surpassing the limit of around €30 000 per QALY. Further, the effectiveness has to be reduced with more than the standard deviation in order to let the standard treatment appear as more effective as well as cheaper. It may thus be concluded that the results presented in the base case give a credible picture of the situation, at least with respect to direct cost and quality-of-life estimates.

It should of course be remembered that the results are based on the data obtained from a clinical trial, and real-life results are seldom exactly the same. Also, some important aspects of the specific immunotherapy have not been touched upon since the data provided by the UKIS trial gave no information. In particular, the effects on slowing down the development of asthma have not been covered (see, e.g. Pajno *et al.*²²).

The value of the productivity loss, both in the standard treatment and with ASQ, is obviously more open to criticism, based as it is on a single study in only one country. This is the reason why we have put more emphasis on the cost-effectiveness ratio for direct costs only, which is not affected by this type of uncertainty. Clearly, better estimates of the number of workdays lost as a consequence of rhinoconjunctivitis, as well as data pertaining to each specific country in the comparison, would improve the quality of the cost-effectiveness ratios estimated in the present paper.

As mentioned earlier, the data on quality of life provided by the clinical trial were designed to shed as much light as possible on the consequences of rhinoconjunctivitis, and were not considered immediately applicable to the assessment of quality of life in terms of general purpose measures such as QALY. The conversion of RQLQ scores to QALYs using the

EQ-5D instrument has two sources of errors, namely (1) incorrect assessment of scores and (2) lack of information on some of the characteristics to be assessed in EQ-5D. Although it seems that the indeterminacy induced by these two circumstances only influences the results to a relatively small extent, it would of course have been preferable if direct assessments in EQ-5D by the patients had been available. It should however be mentioned that the EQ-5D is a somewhat crude instrument, so that even under optimal conditions there is a limit to the possibility of measuring quality of health as more than an approximation which at best is indicative.

With all these reservations, the overall result still gives a rather convincing support for the viewpoint that allergen specific immunotherapy is a treatment which gives value for money, in the sense that the cost of obtaining one QALY – even when the effects on working days registered are not taken into consideration – is sufficiently small to place the treatment among those which should be adopted in the national healthcare systems, as indeed it has been in the countries considered.

As mentioned in the introduction, apart from reporting on the cost-effectiveness of specific allergen immunotherapy we have wanted to compare the cost structure in selected countries. The insight obtained is that there are considerable cost differences.

Looking closer at the figures, one sees that, although a clear pattern is lacking, the main cause of variation is the difference in therapeutic tradition in individual countries. The up-dosing and maintenance treatments are quite costly in some countries and rather cheap in others, as is shown indirectly in Table 6 where we have given the shares of medicine and of other treatment costs in the total direct cost of specific immunotherapy. It can be seen that the variation comes from different practices at the time of up-dosing rather than from the price of the medicine which varies much less between countries. With few exceptions, the cost connected with using scarce medical staff is substantial everywhere, pointing to a potential for improving cost-effectiveness of specific immunotherapy in the future.

Incidentally, this rather surprising country variation confirms the established opinion, according to which cost-effectiveness analyses carried out in one country cannot be passively applied in other countries. Not only is the price structure of one country normally different from that of other countries, but the resource use induced by the price structure and perhaps even more by therapeutic traditions differs as well, and as is shown, quite significantly in some respects. Thus, the emphasis on country-specific cost-effectiveness assessment seems well-founded.

Table 6. Shares of medicine and other expenses in total (direct) cost of immunotherapy, %

	Austria	Denmark	Finland	Germany	Netherlands	Sweden
Medicine	0.79	0.44	0.36	0.79	0.45	0.20
Other cost	0.21	0.56	0.64	0.21	0.55	0.80

Source: Table 2

Conclusion

In this study we have estimated the cost-effectiveness of immunotherapy with ASQ for patients with seasonal allergic rhinoconjunctivitis. The study is based on a clinical study where patients were followed over a year; other studies confirming the findings have followed the patients up to 9 years, and therefore this has been taken as the period over which the patients' behaviour has been projected in our computational model. The results show that immunisation with ASQ is cost-effective, with estimates of cost-effectiveness in the range €10 000–25 000/QALY when measured from the point of view of the healthcare system, and it achieves cost savings when measured from the point of view of society, including the reduced loss of workdays.

Comparing the results obtained for different European countries, a considerable variation is detected, which to some extent may be attributed to different national practices in the up-dosing phase.

Acknowledgement

The research reported in this paper was supported by ALK-Abelló, Denmark.

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 Paper CMRO-3691_2, Accepted for publication: 08 March 2007
 Published Online: 17 April 2007
 doi:10.1185/030079907X187865