

A Cost-Minimisation Analysis Comparing Sublingual Immunotherapy to Subcutaneous Immunotherapy for the Treatment of House Dust Mite Allergy in a Swedish Setting

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Abstract

Background and Objectives In Sweden, approximately 6% of children and 10% of adults suffer from house dust mite (HDM) allergy with symptoms of allergic rhinitis and allergic asthma. Treatment is aimed at reducing HDM exposure and to control the symptoms of allergic rhinitis and allergic asthma by symptom-relieving pharmacotherapy. This pharmacotherapy is often effective, but some patients remain inadequately controlled. For these patients, allergy immunotherapy (AIT, subcutaneous or sublingual) with repeated administration of HDM allergen should be considered. The objective of this study was to compare the costs for sublingual AIT (SLIT; SQ[®] SLIT-tablet) to the costs for subcutaneous AIT (SCIT; SQ[®] SCIT) for the treatment of HDM allergy in a cost-minimisation analysis (CMA).

Methods The CMA included resources (and costs) for treatment, healthcare visits, travelling and lost productivity. Resource use based on Swedish clinical treatment practice and costs were obtained from medical price lists. Analyses were conducted from the societal, as well as healthcare perspective, by use of a time horizon of 3 years.

Results The results show that SQ[®] SLIT-tablet is a cost-saving treatment as compared to SQ[®] SCIT for the

treatment of HDM allergy (€6800 over 3 years). The results are mainly driven by the cost of healthcare visits and the frequency of SCIT administrations.

Conclusion In conclusion, cost-savings of €6800 over 3 years are expected from treating HDM allergy with SQ[®] SLIT-tablet as compared to SQ[®] SCIT, including costs for treatment, healthcare visits, travelling and lost productivity. The reduced number of healthcare visits compensates for higher medication costs.

Key Points for Decision Makers

The difference in costs for sublingual allergy immunotherapy with SQ[®] SLIT-tablet and for subcutaneous allergy immunotherapy (SQ[®] SCIT) was calculated in a cost-minimisation analysis performed from the societal perspective in a Swedish setting.

Sublingual allergy immunotherapy with SQ[®] SLIT-tablet was cost-saving (€6800 over 3 years) as compared to subcutaneous allergy immunotherapy (SQ[®] SCIT), and the major cost-savings were derived from the reduced number of healthcare visits for sublingual therapy.

With sublingual immunotherapy, more patients can be treated at the same cost as those with subcutaneous allergy immunotherapy, and subsequently healthcare resources can be liberated for alternative uses.

Regardless of route of administration, allergy immunotherapy has a large potential for cost-savings by reducing the prevalence of uncontrolled allergic rhinitis and allergic asthma in the society as a whole.

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1 Introduction

Allergy is a systemic disease and symptoms can involve almost any organ of the body. The most prevalent symptoms affect the respiratory system and allergic rhinitis and allergic asthma are increasingly considered as manifestations of a single inflammatory airway syndrome termed respiratory allergic disease [1, 2]. Common features, suggesting a link between these upper and lower airway manifestations, include epidemiological observations, common inflammatory mechanisms, functional aspects, common triggers and therapeutic observations [1]. Both allergic rhinitis and allergic asthma affect the mucosal lining of the respiratory tract, and common underlying cellular processes including a systemic immunoglobulin E (IgE)-mediated immunological response to inhaled allergens are shared [2, 3]. Allergic rhinitis is characterised by symptoms of sneezing, nasal itching, nasal obstruction and nasal discharge and symptoms of allergic asthma include intermittent attacks of breathlessness, wheeze, cough, and chest tightness [4, 5].

House dust mite (HDM) is one of the most common sources of indoor allergens causing allergic rhinitis and allergic asthma [6]. Allergic symptoms due to HDM are triggered by airborne fragments of mite bodies and faecal particles, which reach the respiratory mucosa in sensitised subjects, and result in an allergic immune response [7]. In the Swedish population, allergy to HDM has been estimated at 6% in children and at 10% in adults, as obtained by patient self-reporting of HDM allergy [8].

The symptoms of allergic rhinitis pose a high burden on patients' quality of life. The impact is shown in terms of loss of sleep, fatigue, learning impairment, decreased cognitive functioning and decreased long-term productivity [9]. For asthma in general, the burden of disease has been found to be very broad, affecting social life, personal relationships, employment and finances [10]. In addition, the costs for respiratory allergic disease are high. A recent study on the cost of allergic rhinitis in Sweden reported a total annual cost per patient of Euro (€) 961, ranging from €464 in patients with mild allergic rhinitis to €1757 in patients with moderate/severe disease. This cost included direct costs (pharmacological treatment and healthcare costs) and indirect costs in terms of lost productivity (absenteeism and presenteeism). The total cost of allergic rhinitis in Sweden was estimated at €1.3 billion per year [11]. Likewise, the annual cost of asthma (allergic and non-allergic) in Sweden is substantial, and in a publication from 2007, the total cost of asthma for the population aged 25–56 was estimated at €411 million in 1996 price level. The direct medical costs were mainly driven by medication costs followed by outpatient care and hospitalisations.

Total indirect costs (including disability pension and absenteeism) constituted 69% of the total costs [12].

Symptom-relieving allergic rhinitis and allergic asthma pharmacotherapies are often effective; however, some patients remain inadequately controlled and suffer from residual troublesome and persistent symptoms [13, 14]. For these patients, allergy immunotherapy (AIT) should be considered. AIT differs from symptom-relieving pharmacotherapy by targeting the underlying disease and is the only treatment with the potential to modify the course of disease [15]. Traditionally, AIT has been administered as subcutaneous injections, also called subcutaneous immunotherapy (SCIT). However, SCIT treatment of allergies, including HDM allergy, is associated with high resource use and associated costs for the healthcare sector, and lack of convenience and lost productivity for the patient due to numerous healthcare visits required for SCIT administration [16]. SCIT might also lead to inequality in offered care due to the requirement for administration in specialist centres predominantly found in cities. Consequently, standardised sublingual formulations (sublingual immunotherapy—SLIT), i.e. SLIT-tablets, has been made available for home treatment of grass pollen allergy and recently also HDM allergy (SQ[®] SLIT-tablet; ACARIZAX[®]).

The SQ[®] SLIT-tablet has undergone an extensive clinical trial programme forming the basis for approval in Europe and clinical efficacy and safety. The clinical trial programme included more than 5000 patients with HDM allergic rhinitis and/or allergic asthma [17–22], recently reviewed in a publication by Klimek et al. [23]. As compared to SCIT, SLIT offers a more convenient treatment for the patient, and a reduced burden to the healthcare sector as well as society, as SLIT can be administered by the patient at home following monitored administration of the first tablet in the doctor's office.

To date, no head-to-head comparisons have been made for HDM SLIT-tablet and HDM SCIT products. The standard approach would then be to compare data based on meta-analysis; however, the interstudy heterogeneity in the relatively small HDM SCIT studies would hamper the analysis [24]. Thus, in the lack of stronger evidence, the outcome of studies on HDM immunotherapy with similar study characteristics (including study design, patient selection criteria and scoring of patient-reported outcomes) could be compared. In a publication by Mosbech et al., an HDM SLIT-tablet study was compared to two HDM SCIT studies with similar patient selection criteria. Mosbech et al. concluded that the effect was comparable for the HDM SLIT-tablet and HDM SCIT and that the included studies showed no significant differences in study design, patient population and selection criteria [25]. In addition, it has been shown that AIT, regardless of route of

administration, results in similar immunologic changes, e.g. in the form of increased IgG4-levels [26]. Further supportive information can be found among publications on AIT for the treatment of grass pollen allergy where the two most recent meta-analyses only including SLIT-tablet and SCIT and excluding SLIT-drops concluded that the efficacy of SLIT-tablets and SCIT were comparable [27, 28], while earlier meta-analyses, also including SLIT-drops, were more inconclusive [29, 30] or reported a beneficial effect of SCIT over SLIT [31–33]. The inclusion of SLIT-drops in the meta-analyses could have contributed to higher interstudy heterogeneity, increasing the uncertainty of the analysis.

In conclusion, although limited, current evidence suggest that the efficacy of the HDM SLIT-tablet is comparable to the efficacy of HDM SCIT. Under these circumstances a health economic analysis comparing the SQ[®] SLIT-tablet to SQ[®] SCIT (Alutard SQ[®]) for the treatment of HDM allergy, in the form of a cost-minimisation analysis (CMA) is relevant to conduct.

2 Methods

2.1 Cost-Minimisation Analysis

In a CMA, only the economic consequences of two treatments compared to one another are investigated. In the present analysis, patients with moderate-to-severe HDM allergic rhinitis with or without allergic asthma or HDM allergic asthma associated with mild-to-severe allergic rhinitis not well controlled despite use of symptom-relieving treatments (e.g. antihistamines and inhaled asthma medications) are included (in accordance with the indication for AIT treatment of HDM allergy). The modelled

patients can either be treated with once daily oral SQ[®] SLIT-tablet or with SQ[®] SCIT up-dosed with weekly injections for seven weeks followed by injections every 6 weeks during the maintenance phase (common practice in Sweden).

The analyses are performed over 3 years, which is consistent with the recommended duration and common practice for both treatments in Sweden. As the outcome in terms of efficacy and safety, during as well as after treatment, is assumed to be equal for both treatments, this time span is long enough to capture all relevant costs for the two treatments.

The following resources are included in the analyses: AIT medications (SQ[®] SLIT-tablet and SQ[®] SCIT), healthcare resource use (monitoring and administration of treatment), patient travelling and lost productivity for healthcare visits. Thus, a societal perspective is applied to the analyses, but results will also be presented from a healthcare perspective only including medication and treatment costs. A model overview is presented in Fig. 1.

Concomitant medication resource use in the form of symptom-relieving treatments have not been included in the analysis. It is assumed that these treatments are reduced to the same extent by SQ[®] SLIT-tablet and SQ[®] SCIT treatment as equal efficacy are assumed for the two treatments. Likewise, resource use for the treatment of adverse events including mainly local allergic reactions especially in the mouth for SQ[®] SLIT-tablet and around the injection site for SQ[®] SCIT have not been included in the analysis.

2.2 Resource Use

The healthcare resources used for the treatment (medications and healthcare visits) were identified and quantified together with non-healthcare resources including patient

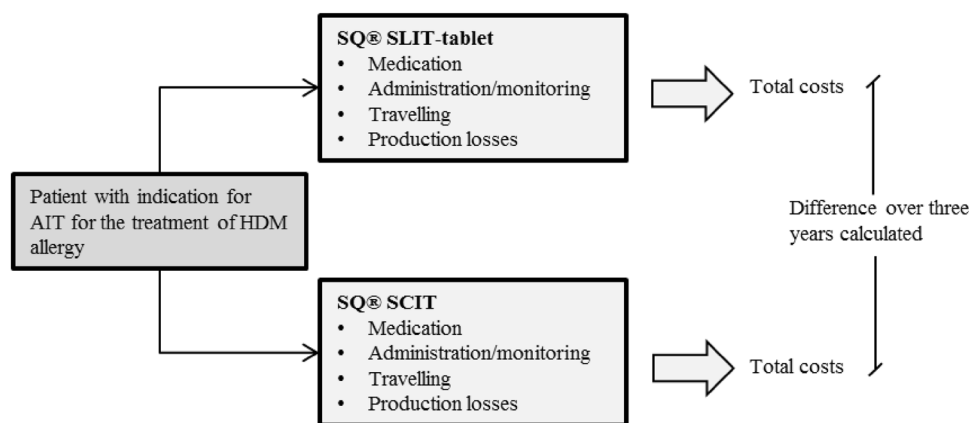


Fig. 1 Cost-minimisation analysis model overview. In the model patients indicated for allergy immunotherapy (AIT) for house dust mite (HDM) allergy can be treated with either sublingual immunotherapy (SLIT) or subcutaneous immunotherapy (SCIT). In

the model the total costs for medication, administration/monitoring of medication, travelling and production losses are calculated over 3 years and compared

travelling and production losses. The identification and quantification of healthcare resources were based on clinical practice and treatment regimens described in The Summary of Product Characteristics (SPC) for SQ[®] SLIT-tablet and SQ[®] SCIT [34, 35]. In the Swedish setting, it is assumed that all patients treated with AIT regardless of route of administration are treated by an allergist or otolaryngologist as AIT is rarely performed by general practitioners in Sweden.

Resources used for patient travelling was estimated based on a publication from the World Health Organisation: The World Health Survey country report for Sweden in which the mean travelling time to secondary care (in terms of hospitalisation) was investigated in 1000 Swedish patients and reported to be an average of 35 min [36].

Patient lost productivity for healthcare visits (monitoring and administration of medication) was also included in the analyses. It is assumed that for each visit to the healthcare sector the patient will lose 2 h of work based on the estimated travelling time to and from the healthcare facility and an expected visit time of 50 min, including parking and waiting time [36]. It is assumed that 70% of the patients are in their productive ages based on data from The Swedish Prescribed Drug Register (include data on all prescribed medications purchased by the patient in Sweden). Data on the age for all patients purchasing medication with the ATC code V01AA03 (allergen extracts, HDM) during 2007 were collected, showing that 70% of the patients were in their productive ages (20–64 years) [37].

More details on the quantification of resources used are given in Table 1.

The analyses only include patients who complete the 3-year treatment course for SQ[®] SLIT-tablet and SQ[®] SCIT. However, to account for the fact that early discontinuation will occur for both treatments, extra resource use in terms of medication used by patients discontinuing treatment early has been added to the resources used by patients completing the treatment. Data from The Swedish Prescribed Drug Register were used to estimate the resource use for early discontinuation [37]. As no data are available for the SQ[®] SLIT-tablet for the treatment of HDM allergy, data for the SQ[®] SLIT-tablet and SQ[®] SCIT for the treatment of grass pollen allergy were used as a proxy, and all new patients starting treatment in 2007 were identified. The patients' medication purchases were followed for 3 years, and the number of patients completing ($n = 202$ for SQ[®] SCIT and $n = 348$ for SQ[®] SLIT), as well as discontinuing treatment early ($n = 152$ for SQ[®] SCIT and $n = 288$ for SQ[®] SLIT), were gathered. In addition, the total number of packages purchased by patients discontinuing treatment early was calculated together with the total cost for these packages (total cost of €47,724 for SQ[®] SCIT and €178,834 for SQ[®] SLIT). Based on these numbers, an additional per patient

cost was calculated by dividing the total cost for medication purchased by patients discontinuing treatment early with the total number of patients completing treatment. With this procedure, an extra cost of €514 (178,834/348) per patient treated with SQ[®] SLIT-tablet and €236 (47,724/202) per patient treated with SQ[®] SCIT was estimated and utilised in the analyses.

2.3 Unit Costs

Unit costs were gathered from publicly available price lists, The Swedish Tax Agency and Statistics Sweden, and are described in detail in Table 1 together with total costs [38–43]. Costs were obtained in Swedish kronor (SEK) but converted into € using the average exchange rate for 2015 (€1 = SEK 9.36). Costs were reported in 2015 price level and costs incurred during the second and third year were discounted 3% annually according to Swedish guidelines [44].

2.4 Sensitivity Analyses

Univariate sensitivity analyses were performed by varying the input values for included parameters one by one $\pm 25\%$ of base-case value (healthcare visit unit cost; patient travelling unit cost and distance; lost productivity unit cost, number of hours lost from work and percent of patients being in their working ages; and discounting). In addition, one scenario analysis—analysing the impact on cost-savings if SQ[®] SCIT is administered every 8 weeks instead of every 6 weeks in maintenance phase—was conducted. In another scenario analysis, the extremes of varying all parameters included in the univariate sensitivity analyses simultaneously by $\pm 25\%$ of base-case value, were tested.

3 Results

3.1 Base-Case Results

The base-case results from a societal perspective are presented in Table 2, showing that treatment of HDM allergy with SQ[®] SLIT-tablet will constitute a cost-saving alternative as compared to SQ[®] SCIT over 3 years in the Swedish setting. The total costs for SQ[®] SLIT-tablet treatment amounts to €5100 over 3 years. The corresponding cost for SQ[®] SCIT is €11,900. Consequently, the total cost-savings are approximately €6800. For each patient treated with SQ[®] SCIT, 2.3 patients could be treated with SQ[®] SLIT-tablet at the same cost.

The difference in travelling costs (cost-savings of approximately €400 over 3 years) and costs of early discontinuation (additional cost of approximately €300 over 3 years) for SQ[®] SLIT-tablet as compared to SQ[®] SCIT

Table 1 Resource use, unit costs and total costs (undiscounted)

Resource	Resource use	Unit cost (€)	Total cost (€)	Reference	Comment
SQ [®] SLIT-tablet	One SQ [®] SLIT-tablet daily for 3 years	3.18–3.57 per tablet (package containing 90 tablets and 30 tablets, respectively)	1172 year 1 and 1161 per year the second and third year	ALK, SPC [34]	One package containing 30 tablet used for the first 30 days of treatment is followed by usage of packages containing 90 tablets for the remaining treatment period
SQ [®] SCIT	Up-dosing during 7 weeks (total of 11 injections) Maintenance treatment every sixth weeks for 3 years (seven injections year 1, nine injections year 2, nine injections year 3)	12.99 per injection 25.15 per injection (maintenance vial and up-dosing vial, respectively)	143 for up-dosing phase 152 for maintenance year 1, 226 per year the second and third year	ALK and SQ [®] SCIT SPC [35]	It is assumed that the last vial in the up-dosing kit is used for the first two injections in maintenance. For maintenance treatment, it is assumed that each vial covers five injections. The price formerly reimbursed is used in the analyses (the price of SQ [®] SCIT has been increased after removal from the Swedish reimbursement system in 2013)
Visit specialist—SQ [®] SLIT-tablet	Two visits year 1, one visit per year in years 2 and 3	257.80 per visit	516 year 1, 258 per year the second and third year	Price lists county councils [38, 39, 42]	Assumption on number of visits in accordance to Swedish clinical practice. Unit cost is the mean for visits to allergist/otolaryngologist for the three largest county councils in Sweden
Visit specialist—SQ [®] SCIT	18 visits year 1, 9 visits year 2, 9 visits year 3		4640 year 1, 2320 per year the second and third year		Each injection requires one visit. Unit cost is the mean for visits to allergist/otolaryngologist for the three largest county councils in Sweden
Travelling to/from visits—SQ [®] SLIT-tablet	30 km per one-way trip to specialist. 120 km year 1, 60 km year 2, 60 km year 3	1.98 per 10 km	24 year 1, 12 per year the second and third year	World Health Survey and The Swedish Tax Agency [36, 43]	Distance travelled is based on published average time travelled to specialised healthcare in Sweden 2003 (35 min) and an assumption on a speed of 50 km/h
Travelling to/from visits—SQ [®] SCIT	30 km per one-way trip to specialist. 1080 km year 1, 540 km year 2, 540 km year 3		214 year 1, 107 per year the second and third year		
Lost productivity—SQ [®] SLIT-tablet	2 h per visit. 4 h year 1, 2 h year 2, 2 h year 3	30.36 per hour	121 year 1, 61 the second and third year	Statistics Sweden and The Swedish Tax Agency [40, 41]	Two hours per visit assumed. Total visit time of 50 min assumed. Travelling 35 min × 2
Lost productivity—SQ [®] SCIT	2 h per visit. 36 h year 1, 18 h year 2, 18 h year 3		1093 year 1, 547 the second and third year		

SQ[®] SLIT sublingual immunotherapy, SQ[®] SCIT subcutaneous immunotherapy

are limited as compared to the other costs included in the analysis from the societal perspective.

Analyses performed from the healthcare perspective, only including costs for medications and healthcare visits, results in cost-savings of approximately €5400 over 3 years. For SQ[®] SLIT-tablet the cost for medication and healthcare visits is €4400 and for SQ[®] SCIT is €9800 over 3 years. The higher medication cost for SQ[®] SLIT-tablet as compared to SQ[®] SCIT (€2700 more expensive over

3 years) is by far compensated by the cost-savings (€8100) obtained from fewer healthcare visits (a total of four visits for SQ[®] SLIT-tablet as compared to a total of 36 visits required for SQ[®] SCIT over 3 years).

3.2 Sensitivity Analyses

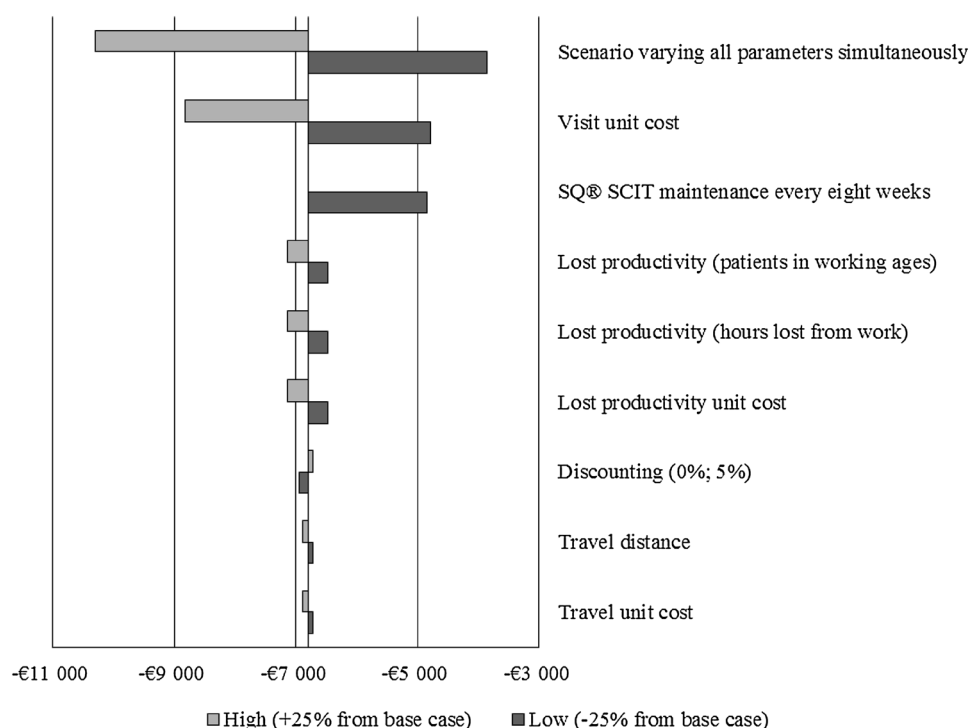
The results of the univariate sensitivity analyses and scenario analyses are presented in Fig. 2. The two

Table 2 The total costs of SQ[®] SLIT-tablet and SQ[®] SCIT treatment of house dust mite allergy in Sweden over 3 years

Cost item	SQ [®] SLIT-tablet (€)	SQ [®] SCIT (€)	Difference (€)
Direct medical costs	4402	9781	−5380
Drug costs	3393	701	2692
Healthcare visit costs	1009	9080	−8071
Direct non-medical costs	46	418	−371
Travelling costs	46	418	−371
Indirect costs	166	1497	−1331
Lost productivity	166	1497	−1331
Cost of early discontinuation	514	236	278
Total	5129	11,933	−6804

SQ[®] SLIT sublingual immunotherapy, SQ[®] SCIT subcutaneous immunotherapy

Fig. 2 Results of the sensitivity analyses presented in a tornado diagram. Resulting cost-savings over 3 years from the societal perspective for sublingual immunotherapy (SLIT) as compared to subcutaneous immunotherapy (SCIT) for different univariate sensitivity analyses and scenario analyses are shown in the diagram. Base case cost-savings of €6804 are indicated by the vertical, middle line of the tornado diagram



parameters with the largest impact on the results are the cost of specialist visits for monitoring and administration of treatment as well as the frequency of administration of SQ[®] SCIT in the maintenance phase of treatment. When the specialist visit unit-cost was varied by $\pm 25\%$ (corresponding to change of €64), the total resulting cost-savings derived from treating HDM allergy with SQ[®] SLIT-tablet as compared to SQ[®] SCIT ranged from approximately €4800 to €8800 (change of $\pm 30\%$ from base case). If SQ[®] SCIT is administered every 8 weeks (corresponding to a total of 29 injections) instead of every 6 weeks (corresponding to a total of 36 injections) in maintenance phase, the cost-savings obtained from treatment with SQ[®] SLIT-tablet would be reduced to approximately €4800 over 3 years (29% lower cost-savings as compared to the base-case analysis).

In the scenario analysis testing the extremes (setting all parameter input values to $\pm 25\%$ of base case simultaneously) the total cost-saving derived from treating HDM allergy with SQ[®] SLIT-tablet as compared to SQ[®] SCIT ranged from approximately €3900 to €10,300.

For all analyses performed, the resulting cost-savings obtained from treating HDM allergy with SQ[®] SLIT-tablet as compared to SQ[®] SCIT are close to or above €4000 for the analysed 3-year period.

4 Discussion

In this CMA, the economic consequences of treating HDM allergy with SQ[®] SLIT-tablet or SQ[®] SCIT were compared. Equal efficacy of the two treatment alternatives was

assumed and under these circumstances treatment with SQ[®] SLIT-tablet is a cost-saving alternative from the societal as well as the healthcare perspective. The cost-savings amounted to €6800 and €5400 over 3 years from the societal and healthcare perspective, respectively. These results imply that cost-saving could be made by initiating patients with HDM allergy with an indication for AIT on SQ[®] SLIT-tablet rather than SQ[®] SCIT, or alternatively, that more patients could be treated with AIT or that healthcare resources could be reallocated.

Patients suffering from HDM allergy often have concomitant allergies. A substantial number of patients allergic to HDM might therefore require additional AIT treatment, including also a second (and possibly third) allergen. Theoretically, based on the results above, AIT treatment with two different allergens in the form of SLIT-tablets would still be cost-saving as compared to parallel treatment with two different SCIT allergens, even though the medication costs would be doubled.

The univariate sensitivity analyses performed show that the results are robust, and in all analyses performed treatment with SQ[®] SLIT-tablet will constitute a cost-saving alternative as compared to treatment with SQ[®] SCIT. The resulting cost savings were close to or above €4000 over 3 years for all analyses. The main driver of the results is the number of healthcare visits needed for administering SQ[®] SCIT or the unit cost for these visits. By changing the input value for the unit cost by $\pm 25\%$ (corresponding to a change of approximately €64), the resulting cost-savings obtained from treatment with SQ[®] SLIT-tablet as compared to SQ[®] SCIT will be changed by $\pm 29\%$ (corresponding to a change of €2000 from the base-case results over 3 years). When the frequency of SQ[®] SCIT maintenance phase injections are changed from every 6 weeks to every 8 weeks (total number of visits reduced from 36 to 29 visits for SQ[®] SCIT) the cost-saving will be reduced by 30% (corresponding to a change of €2000 from the base-case results over 3 years). However, data gathered by ALK and The Swedish Dental and Pharmaceutical Benefits Agency for SCIT treatment of grass pollen allergy show that injections every 6 weeks is the average interval between injections routinely used in clinical practice in Sweden [45]. The unit cost of €258 for specialist healthcare visits included in the analyses is the average of published visit costs to an allergist or otolaryngologist in the three largest county councils in Sweden. Hypothetically, this unit cost could be as low as €41 and cost-neutrality would still result for the two treatment options SQ[®] SLIT-tablet and SQ[®] SCIT when the analyses are performed from a societal perspective.

As already noted, the societal costs of allergy in the form of allergic rhinitis and asthma are high in Sweden [11, 12]. Hence, treatments that have the potential to

decrease the prevalence of uncontrolled allergic rhinitis and allergic asthma are highly important and extensive societal savings could be expected from increasing the number of AIT-treated patients. The findings in the present CMA are supported by a review reporting cost savings associated with SLIT-tablet treatment as compared to SCIT treatment in four out of six included studies. The studies were performed in Europe and North America and included AIT for the treatment of different seasonal and perennial allergies [15]. The findings in the present study are further substantiated by a recently published Danish study reporting on cost savings (approximately €3000) for SQ[®] SLIT-tablet as compared to SQ[®] SCIT for the treatment of HDM allergy including direct and indirect costs over 5 years of treatment. When only medication costs and healthcare visit costs were included in the analysis, the cost-savings were more limited and amounted to approximately €700 over 5 years in the Danish setting [16]. Together, the results of the CMAs presented above imply that the findings in the present analysis could be relevant also outside the Swedish setting, considering the extensive number of healthcare visits that can be saved and the accompanying reduced lost productivity when SLIT is administered instead of SCIT. Consequently, cost-savings can be expected from the societal as well as the healthcare perspective, assuming comparable efficacy for SLIT and SCIT.

The performed CMA is associated with some limitations. The cost of adverse events has not been included in the analyses. This could be a conservative approach as there are studies suggesting that the adverse event profile is more beneficial for SLIT treatment as compared to SCIT treatment [46, 47]. In addition, publicly available price lists were used for unit cost input in the analyses and may not accurately reflect the opportunity cost (value of forgone benefits due to alternative use of resources not being available), which should ideally be used in a health economic analysis. This was, however, considered to be the best available substitute for the opportunity cost. The inclusion of costs for patients discontinuing treatment early was based on data for AIT treatment for grass pollen allergy and should ideally have been based on data on the treatment of HDM allergy instead.

SLIT-tablet treatment constitutes a more convenient approach to the patient by heavily reducing the number of healthcare visits required. This could, however, be at the expense of reduced compliance and/or persistence, which has not been accounted for in the performed CMA. Nevertheless, some studies, including a Swedish study, have found that patient compliance and/or persistence to SLIT-tablet and SCIT treatment are similar [48, 49], as opposite to other studies where the compliance and persistence rates have been reported to be lower for SLIT-tablet treatment

[50]. The rate of compliance and/or persistence will impact the equal effectiveness assumption, which will only hold true if these rates are the same or similar for the two compared treatment options.

In conclusion, treatment with SQ[®] SLIT-tablet constitutes a cost-saving alternative as compared to SQ[®] SCIT for the treatment of HDM allergy in a Swedish setting from a societal as well as a healthcare perspective. Reducing the prevalence of uncontrolled allergic rhinitis and allergic asthma in the society as a whole has a large potential for extensive cost savings, and these cost savings should be increased by initiating treatment with SQ[®] SLIT-tablet instead of SQ[®] SCIT under the assumption that both treatments are equally effective.

Compliance with Ethical Standards

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Conflicts of interest Åse Björstad is employed by Nordic Health Economics AB, which received a fee for services related to the development and execution of this study, and for the analysis, and reporting of its results. Lars-Olaf Cardell has received grants, consulting honorariums, travel grants and an honorarium for his contributions to evaluating this study and to the development of this manuscript, all from ALK. Julie Hahn-Pedersen was an employee of ALK during development of this manuscript and has stock options in ALK. Mikael Svärd is employed by ALK.

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