ClinicoEconomics and Outcomes Research

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Modelling the Costs of Sublingual Immunotherapy versus Subcutaneous Immunotherapy Based on Clinical Appointments and Impacts of Patient Travel in Sweden

Lars-Olaf Cardell[1,2,*], Thomas Sterner[3,*], Waqas Ahmed[4], Andreas Kallsoy Slættanes[5], Mikael Svärd[6], Richard F Pollock[4]

[1]Division of ENT Diseases, Department of Clinical Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden; [2]Department of Otorhinolaryngology, Karolinska University Hospital, Stockholm, Sweden; [3]Department of Economics, School of Business, Economics and Law, University of Gothenburg, Gothenburg, Sweden; [4]Covalence Research Ltd, Harpenden, UK; [5]ALK, Hørsholm, Denmark; [6]ALK Nordic, Kungsbacka, Sweden

*These authors contributed equally to this work

Correspondence: Richard F Pollock, Email pollock@covalence-research.com

Aim: In Sweden, allergy immunotherapy (AIT) is available as either subcutaneous immunotherapy (SCIT) injections or sublingual immunotherapy (SLIT) tablets and is used to treat moderate-severe allergic rhinitis (AR). This study sought to determine direct and indirect annual costs stemming from treatment-related travel, appointments, waiting times and medication costs, before exploring likely CO_2 emission-related cost-savings for 20,330 patients receiving SCIT or SLIT-tablets in Sweden.

Methods: A model was developed in Python to capture each category of costs in the target patient population. Absenteeism costs arising from treatment-related travel were determined by obtaining average hourly pay data from Swedish Government sources. Absenteeism costs were also calculated for 30-minute post-dose observation times, which occurred during one clinical appointment for SLIT patients, and all clinical appointments for SCIT patients. Clinical appointment costs were obtained from healthcare price lists for Sweden. Medication costs were retrieved from the Pharmaceutical Specialities in Sweden (Fass) website, and treatment doses required for SCIT and SLIT-tablets were determined based on product labels and previously-calculated dosage regimes. High-cost protection and reimbursement scheme payment caps were applied when determining patient appointment and medication costs, respectively, and when identifying financial burdens for individual payers.

Results: Mean total annual costs for SCIT were Swedish Krona (SEK) 604.1 million (m), with clinical appointments contributing the largest share of these costs (52.7%), followed by medication (34.4%), travel-related absenteeism (8.9%), waiting time-related absenteeism (2.7%) and private transportation (1.3%). Mean total annual costs for SLIT-tablets were SEK 336.2m. Medication contributed the most to these costs (72.3%), followed by clinical appointments (22.7%), travel-related absenteeism (3.8%), waiting time-related absenteeism (0.6%) and private transportation (0.6%).

Conclusion: For patients with moderate-severe AR receiving AIT in Sweden, SLIT-tablets displayed large potential cost savings to patients, the healthcare system, and the government, whilst possessing reduced societal costs of carbon emissions relative to SCIT.

Keywords: allergic rhinitis, costs, subcutaneous immunotherapy, sublingual immunotherapy

Introduction

Allergic rhinitis (AR) is the most common chronic disease in Sweden.[1] Classic symptoms of AR include nasal discharge, sneezing, nasal itching and nasal congestion, and are brought on by allergens from the environment stimulating inflammatory and immune processes.[2–4] Additionally (although often not as well acknowledged) these patients can also suffer from inflammatory fatigue, as well as tiredness caused by impaired sleep.[5] The disease can significantly impact patients' social activities, productivity and quality of life (QoL), particularly in people with moderate-severe

Received: 6 February 2024
Accepted: 18 May 2024
Published: 10 June 2024

AR.[6–8] Whilst the prevalence of AR in Sweden is estimated at 25%,[9] evidence suggests that this rate is increasing,[6] demonstrating that the clinical and financial burden of the disease is also likely to grow in the future.

The current financial burden of AR is already significant for patients, healthcare systems and governments.[2] In Sweden, the cost of AR in 2016 was estimated to be 1.3 billion Euros (EUR).[10] Presenteeism costs contributed the most to this figure, followed by pharmacological treatment costs.[10] One study focused specifically on estimating costs associated with productivity losses due to AR, with said costs amounting to a figure of EUR 2.7 billion per year.[11]

For people with moderate-severe AR, for whom symptom-relieving medications are insufficient to obtain symptom control,[12] allergy immunotherapy (AIT) is currently the only existing disease-modifying treatment, available in the form of subcutaneous immunotherapy (SCIT) injections or sublingual immunotherapy (SLIT) tablets. Indeed, AIT can alleviate symptoms and reduce the need for further treatment, with these effects persisting after completion of the treatment course.[13]

AIT is effective in patients with moderate-severe AR regardless of the administration route, and the choice of SCIT versus SLIT can therefore be informed, at least in part, by a comprehensive evaluation of the overall value of both SCIT and SLIT-tablets to patients, healthcare systems, governments and wider society. However, each dose of SCIT must be administered within a specialized AR clinic, under the supervision of a clinician, and requires recipients to undergo a 30-minute observation time due to the risk of anaphylaxis.[14] Conversely, individuals taking SLIT-tablets can take their daily doses at home (after the initial dose has been taken under clinician supervision), thereby removing the necessity for much of the treatment-related travel associated with SCIT. Whilst the relative clinical benefits of both treatments have been investigated previously,[15,16] there is still a need to characterize the costs associated with SCIT and SLIT-tablets. In conventional cost-utility analyses, direct costs of health (eg, appointment and medication costs) are often weighed against effectiveness outcomes such as quality-adjusted life years to determine the most cost-effective treatment for a particular disease. However, beyond the direct medical costs, it is often also desirable to consider other cost drivers, including absenteeism arising from travel and clinical appointments, and private transport costs. Furthermore, due to a growing interest by healthcare technology agencies to promote sustainable healthcare interventions, as well as a recent and increased general focus on the global environmental footprint of healthcare, potential societal costs due to CO_2 emissions (arising from patient travel) are also desirable to consider.[17–19] Calculating and discussing these additional costs can serve to demonstrate the financial value of current AIT options to a wide variety of stakeholders, whilst determining if SLIT-tablets hold any impactful cost-saving benefits over SCIT.

The aims of this study were therefore to quantify the total direct and indirect costs for SCIT and SLIT-tablets, when considering a) absenteeism due to treatment-related travel times and clinician appointments, b) private transport, c) clinical appointments and d) medication, before briefly exploring the potential societal impact of CO_2 emissions arising from patient travel. The transportation- and CO_2 emissions-related portions of the analysis were based on the model previously outlined in Cardell and Sterner et al,[17] with additional relevant cost parameters layered onto the model for the purposes of this study.

Methods

Overview of Travel Algorithm

A detailed description of the original travel algorithm, its assumptions, and the data inputs used to determine CO_2 emissions and patient travel times can be found in Cardell and Sterner et al.[17] Briefly, the initial travel algorithm was developed in Python (version 3.10.4). The algorithm identified the closest of 105 specialized AR treatment centers to the representative point (ie, the center) of each of the 290 Swedish municipalities. Once the closest AR treatment center was identified for each municipality, the haversine distance ("straight-line" distance over a sphere) from the representative point to the nearest specialized AR center was determined, adjusted using a relevant detour index and weighted by the municipality population. Transport modality data, including average speeds and CO_2 emissions were then layered on top of the underlying model. The model was run over 1000 iterations using random sampling of detour indexes, with separate mean total CO_2 emissions and travel times estimated for SCIT and SLIT-tablet patients from two separate cohorts, which are described in more detail later on.

Relevant cost parameters were then included in the model for each cohort, with details of these cohorts and parameters outlined in the sections below. Results for each cost category were determined and reported as a mean annual total figure for the one-year cohort, and as a per-patient figure for the three-year cohort. For cost categories that depended on the detour index sampling to determine results, and therefore yielded unique figures per model iteration (ie, private transport costs and travel time-related absenteeism), standard deviations were also determined and reported.

One-Year Cohort Regimes

The one-year "snapshot" cohort comprised 20,330 patients with moderate-severe AR receiving AIT in any given year.[20] This figure comprised 11,730 patients receiving SLIT-tablets and 8600 patients receiving SCIT. For this analysis, all 20,330 patients were modelled as receiving either SCIT or SLIT-tablets. For SLIT-tablets, all patients were assumed to receive one tablet per day for the entire one-year period.[21] For SCIT patients, 1952 patients (9.6%) were assumed to have been recently diagnosed with moderate-severe AR and were modelled as receiving the titration regimen.[17] The remaining 18,378 patients (90.4%) were modelled as receiving maintenance therapy. Details of the titration and maintenance therapy allocation methods, as well as respective dosage details of SCIT regimes simulated in the model have been previously reported in Cardell and Sterner et al.[17] However, a summary of the SCIT treatment funnel for the one-year "snapshot" cohort can be found in Supplementary Figure S1.

Three-Year Cohort Regimes

The three-year "incident" cohort comprised 1000 hypothetical patients, all assumed to be recently diagnosed with moderate-severe AR. The three-year period was chosen to simulate following the patient cohort over one full AIT treatment course. For SLIT-tablets, all patients were again modelled to receive one tablet per day for the entire three-year period.[21] For SCIT, all patients were assumed to start on titration therapy at the beginning of the first year, with completion of the full treatment course (titration and maintenance therapy) taking place over the subsequent three-year period. Regarding titration regimes, 50% of SCIT patients were modelled to receive the 7-week titration regime, with the other 50% of patients modelled to receive the 15-week titration regime.[17,22] A summary of the SCIT treatment funnel for the three-year "incident" cohort can be found in Supplementary Figure S2.

Clinician Appointments: One-Year Cohort

For SLIT-tablet patients, the total number of appointments for the entire cohort equaled 40,660, based on the assumption of two clinical appointments per patient per year. The first appointment involved the patient taking a clinician-supervised dose, before being observed for a 30-minute time period. The second appointment involved a simple follow-up, with no associated supervised dose or observed wait time. For SCIT patients, a total of 169,634 appointments were required, with each patient (on average) attending 8.3 appointments.[17] All 169,634 appointments for SCIT were for SCIT administration, each necessitating a 30-minute post-dose observed wait time. A cost of 1878 Swedish Krona (SEK) was modelled for each clinician appointment, based on the medical treatment for lung and allergy (excluding pulmonary embolism) price from the 2021 Prislista Västra Sjukvårdsreg.[23] However, each patient would only pay a maximum of SEK 1300 per year for appointments, with the remainder of appointment costs being reimbursed by the Swedish government, as per the 2023 high-cost protection for outpatient care scheme.[24]

Clinician Appointments: Three-Year Cohort

For patients receiving SLIT-tablets, a total of 4000 appointments were required, based on the model assuming four clinical appointments per patient over three years. Only the first appointment involved the patient taking a clinician-supervised dose, and a subsequent 30-minute observation period. The three remaining appointments involved simple follow-ups, with no associated observed wait time.

For SCIT patients, the total number of appointments equaled 30,500, with each patient (on average) attending 30.5 appointments, higher per annum than the one-year cohort due to all patients receiving and completing titration and maintenance therapy.[17] Again, all appointments were for SCIT administration, with each necessitating a 30-minute post-dose observed wait time. As for the one-year cohort, a per-appointment cost of SEK 1878 was used,[23] alongside

application of the 2023 high-cost protection for outpatient care scheme.[24] This meant that each patient would pay a maximum of SEK 1300 per year (or a total of SEK 3900 over the entire three-year period) for clinician appointments, with the remainder of appointment costs being reimbursed by the Swedish government.

Medication

For SLIT-tablet therapy, medication costs were modelled using publicly available prices for SQ tree SLIT tablets, which were identified to be SEK 2948.66 per 90-tablet pack, resulting in a cost of SEK 32.76 per tablet (or dose).[25] Patients in the one-year cohort were assumed to take 365 doses over the treatment period, with patients in the three-year cohort assumed to take 1095 doses over the treatment period. Each patient receiving SLIT-tablets would only pay a maximum of SEK 2600 per year (or SEK 7800 in total for patients in the three-year cohort) for prescription costs however, based on the 2023 high-cost reimbursement scheme.[26]

For SCIT therapy, medication costs were modelled using publicly available prices for SQ Birch SCIT injections, which were SEK 6772.50 for one titration pack (comprising 4 x 5mL vials)[27] and SEK 5019 for one maintenance pack (comprising one 5mL vial of strength 100,000 SQ-E/mL).[28]

The model assumed that a single SCIT vial could be re-used for multiple sequential doses, provided that the strength of the vial and the remaining volume was suitable for administering the entirety of the next dose. A summary of the total number (and subsequent costs) of titration and maintenance packs assumed to be used by patients in both the one-year and three-year cohorts can be found in Table 1. Given that SCIT therapy is not currently covered by the high-cost reimbursement scheme in Sweden, 100% of medication costs were assumed to be covered by healthcare providers, in this case the specialized AR treatment centers or hospitals administering each SCIT dose.

Private Transport

Private transport considered the costs of fuel (petrol) for patients receiving both SCIT and SLIT-tablets modelled as either taking their own car or motorcycle to each clinical appointment. A cost of 16.37 SEK/liter of petrol was used based on 2021 figures from the Swedish Energy Agency,[29] as well as a fuel consumption of 5.9 liters/100km.[30] The final model therefore used a cost of 0.96 SEK/km. The proportions of patients using each transport modality varied across some specific municipalities,[17] but cars and motorcycles were consistently amongst the most common modes of private transport used for treatment-related travel.

Absenteeism

The human capital approach considers loss of production due to disease and is widely used for estimating indirect costs in health economic analyses.[31,32] Components of the human capital approach include loss of productivity due to absence from work (absenteeism) and reduced productivity at work without absence due to illness (presenteeism).[33] Given that previous studies have reported comparable efficacy of SCIT and SLIT-tablets (and therefore likely similar and minimal

Table 1 Number of Packs Used for Each SCIT Regime

Cohort	Titration Packs	Maintenance Packs	Total Cost (SEK)
One-year (52 weeks)			
7-week titration	1	1	**11,791.5**
15-week titration	1	1	**11,791.5**
Three-year (156 weeks)			
7-week titration	1	4	**26,848.5**
15-week titration	1	4	**26,848.5**

Abbreviation: SEK, Swedish Krona.

impacts due to presenteeism),[15,16] the present study only considered absenteeism costs; specifically, absenteeism due to patients spending time travelling to and from each of their clinical appointments, in addition to the 30-minute observation waiting times for each patient's initial SLIT-tablet dose, and all SCIT doses.

A cost-per-hour of work missed was determined to be SEK 192.90 and was sourced from official figures outlining the average hourly pay of manual workers in the private sector,[34] published by Statistics Sweden. This figure was used in the base case analysis.

Numerous figures exist for hourly pay in Sweden, each of which use various approaches and sources to determine the final monetary figure. Given this, an exploratory sensitivity analysis was conducted which incorporated an alternative figure for cost-per-hour of work missed. This alternative figure was aimed to be representative of manual and non-manual workers, across both public and private sectors. The figure was determined by identifying the average yearly salary (SEK 445,200) for Swedish employees from data published by the Mediation Institute, an authority under the Ministry of Labor.[35] The average yearly salary was then divided by the average actual weekly hours worked (30 hours) multiplied by the total actual work weeks per year (44.4 weeks).[36] Total actual work weeks per year were determined by assuming 247 total working days (based on the 2023 Swedish calendar), and 25 days of annual leave for each patient, based on the 1977 Annual Leave Act.[37] This yielded a final cost-per-hour (based on actual time spent working) of SEK 334.2. Results for the sensitivity analyses are briefly outlined in the discussion section.

Results

Summary of Cost results: One-Year Cohort

For patients receiving SCIT, mean total annual costs amounted to SEK 604.1 million (m). Clinical appointments contributed the most to these costs (52.7%), followed by medication (34.4%), travel-related absenteeism (8.9%) and waiting time-related absenteeism (2.7%). Private transport contributed the least to overall costs (1.3%). A summary of cost contributions per category is presented in Figure 1.

For patients receiving SLIT tablets, mean total annual costs amounted to SEK 336.2m. Medication contributed the most to these costs (72.3%), followed by clinical appointments (22.7%) and travel-related absenteeism (3.8%). Waiting time-

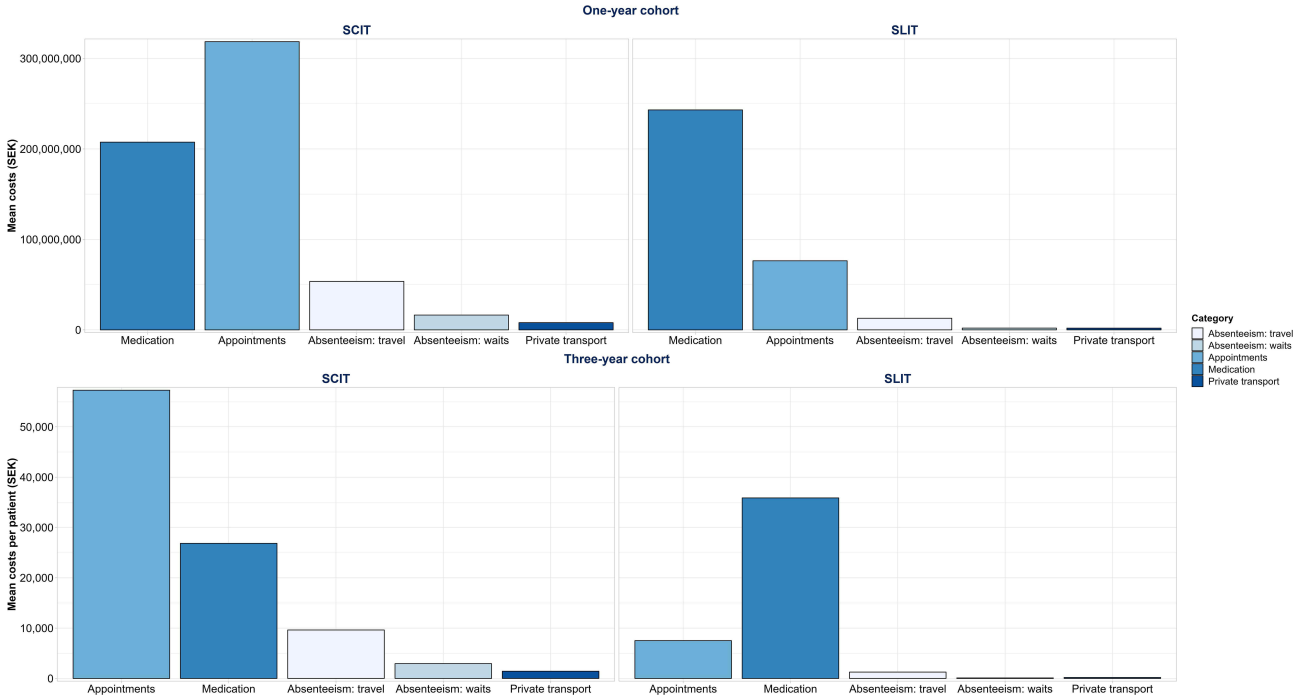

Figure 1 Summary of cost contributions for SCIT and SLIT regimes across both cohorts.
Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

related absenteeism and private transport each contributed 0.6% to overall costs. A summary of cost contributions per category can be found in Figure 1.

Appointment Costs

For patients receiving SCIT, mean total annual appointment costs were SEK 318.6m. Of the SEK 318.6m, SEK 26.4m comprised patient costs, with the remaining SEK 292.1m comprising government reimbursements (see Figure 2).

For patients receiving SLIT tablets, mean total annual appointment costs were SEK 76.4m, 4.17 times lower than SCIT appointment costs. Again, SEK 26.4m comprised patient costs, with the remaining SEK 49.9m comprising government reimbursements (see Figure 2).

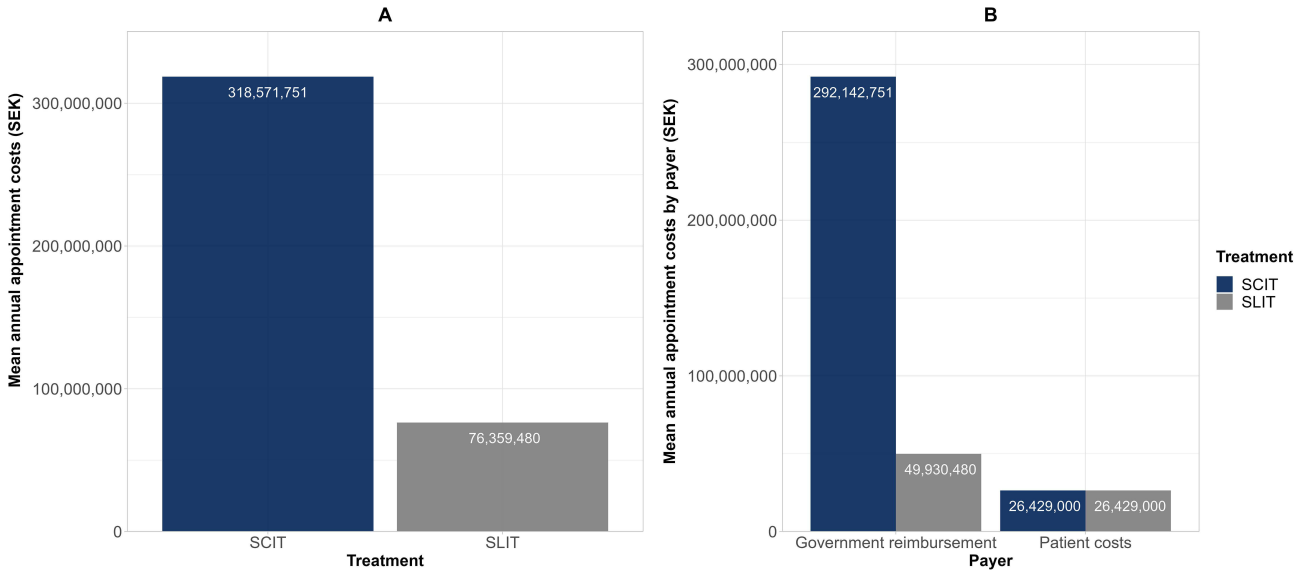

Figure 2 Mean total annual appointment costs (**A**) with payer breakdowns (**B**).
Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

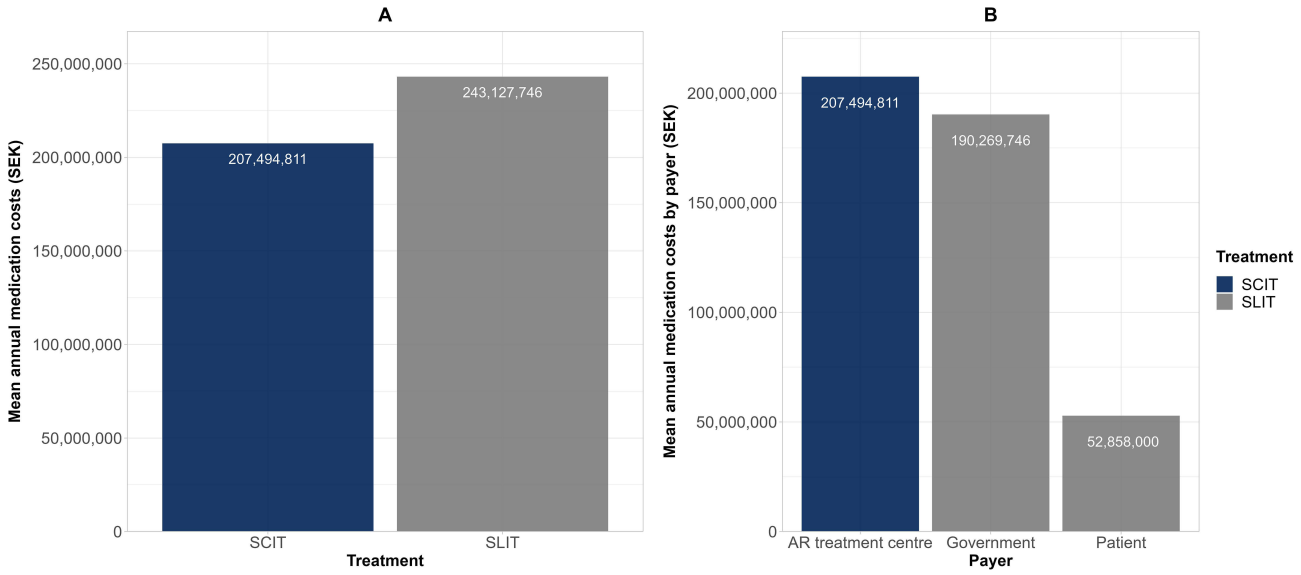

Figure 3 Mean total annual medication costs (**A**) with payer breakdowns (**B**).
Abbreviations: AR, allergic rhinitis; SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

Medication Costs

For patients receiving SCIT, mean total annual medication costs were SEK 207.5m, with 100% of this cost burden falling solely on specialized AR treatment centers, given that SCIT is not covered by the high-cost reimbursement scheme in Sweden (see Figure 3).

For patients receiving SLIT-tablets, mean total annual medication costs were SEK 243.1m, 1.17 times higher than SCIT medication costs). Of the SEK 243.1m, SEK 52.9m comprised patient costs, with the remaining SEK 190.3m comprising government reimbursements (see Figure 3).

Private Transport Costs

For patients receiving SCIT, mean total annual private transport costs were SEK 8m (standard deviation [SD]: SEK 1.7m), with SEK 7.9m arising from private cars (see Figure 4). For patients receiving SLIT tablets, mean total annual private transport costs were SEK 1.9m (SD: SEK 0.4m), 4.21 times lower than SCIT private transport costs. Of the SEK 1.9m, SEK 1.9m arose from private cars (see Figure 4).

Travel-Related Absenteeism

For patients receiving SCIT, mean total annual travel-related absenteeism costs were SEK 53.6m (SD: SEK 11.6m), with SEK 42.2m arising from private car travel (see Figure 5). For patients receiving SLIT tablets, mean total annual travel-related absenteeism costs were SEK 12.8m (SD: SEK 2.8m), 4.19 times lower than SCIT travel-related absenteeism costs. Of the SEK 12.8m, SEK 10.1m arose from private car travel (see Figure 5).

Waiting Time-Related Absenteeism

For patients receiving SCIT, mean total annual waiting time-related absenteeism costs were SEK 16.4m (see Figure 6). For patients receiving SLIT tablets, mean total annual waiting time-related absenteeism costs were SEK 2.0m, 8.20 times lower than SCIT waiting time-related absenteeism costs (see Figure 6).

Summary of Cost results: Three-Year Cohort

For each patient receiving SCIT, mean total costs amounted to SEK 98,000. Clinical appointments contributed the most to these costs (58.4%), followed by medication (27.3%), travel-related absenteeism (9.8%) and waiting time-related

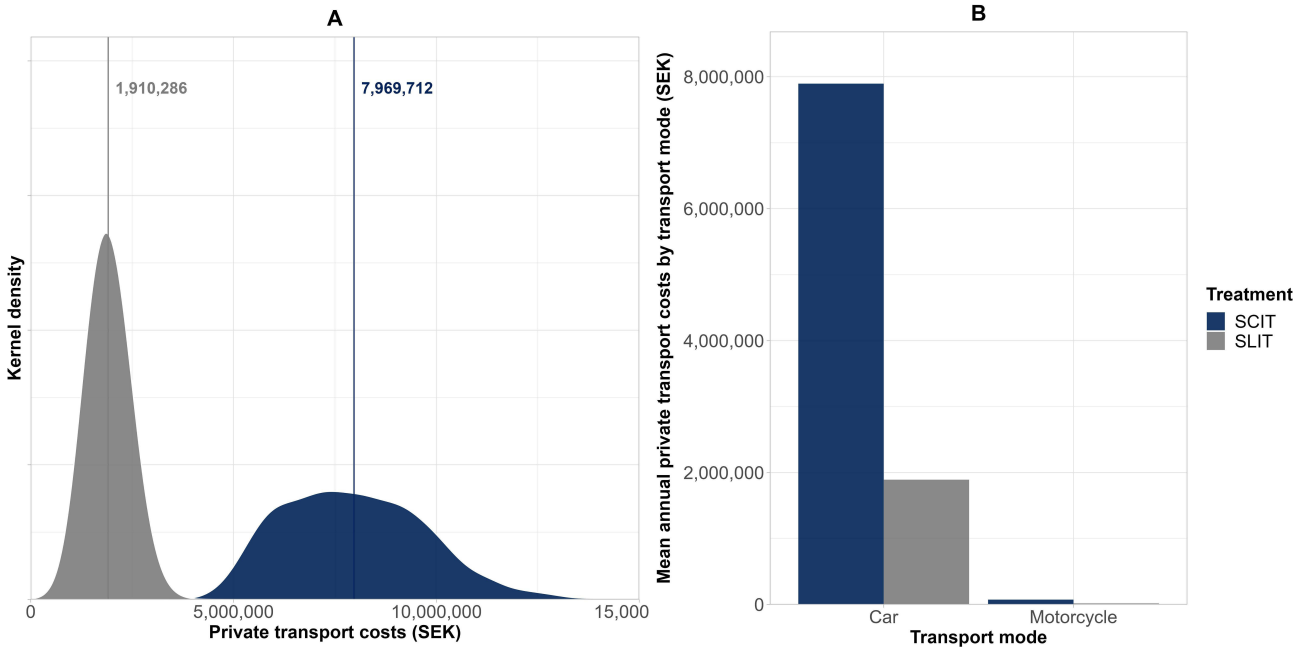

Figure 4 Mean total annual private transport costs (**A**) with transport mode breakdowns (**B**).
Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

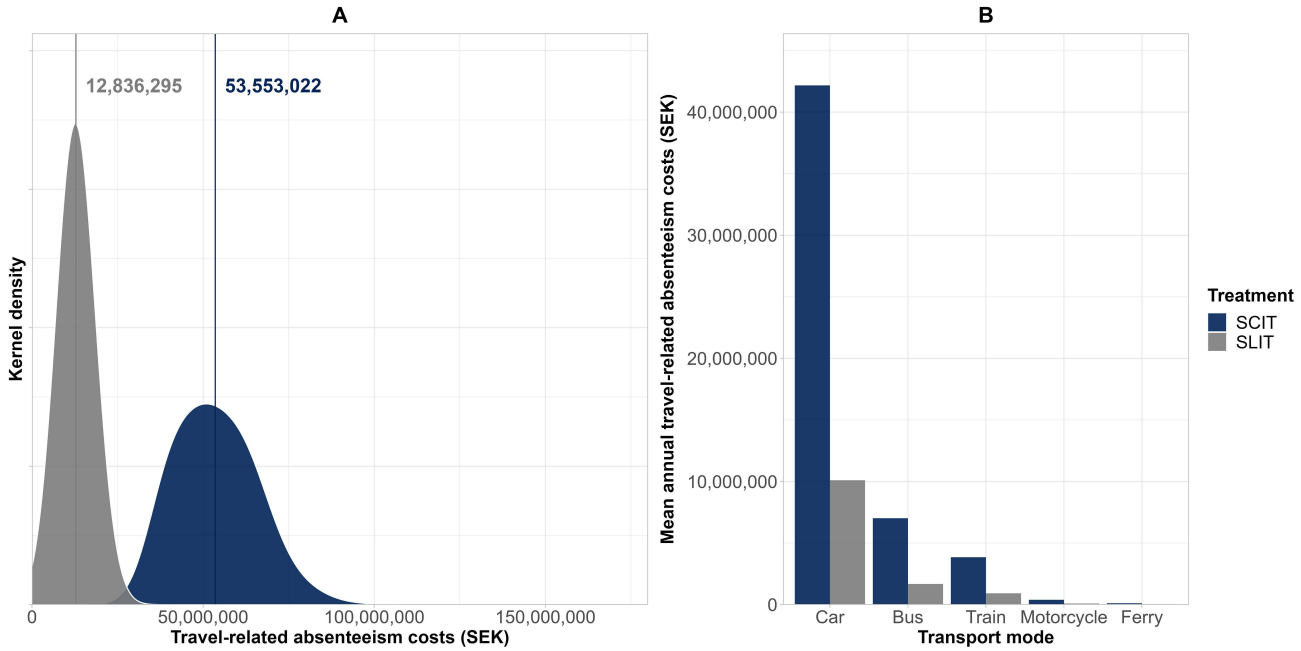

Figure 5 Mean total annual travel absenteeism costs (**A**) with transport mode breakdowns (**B**).
Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

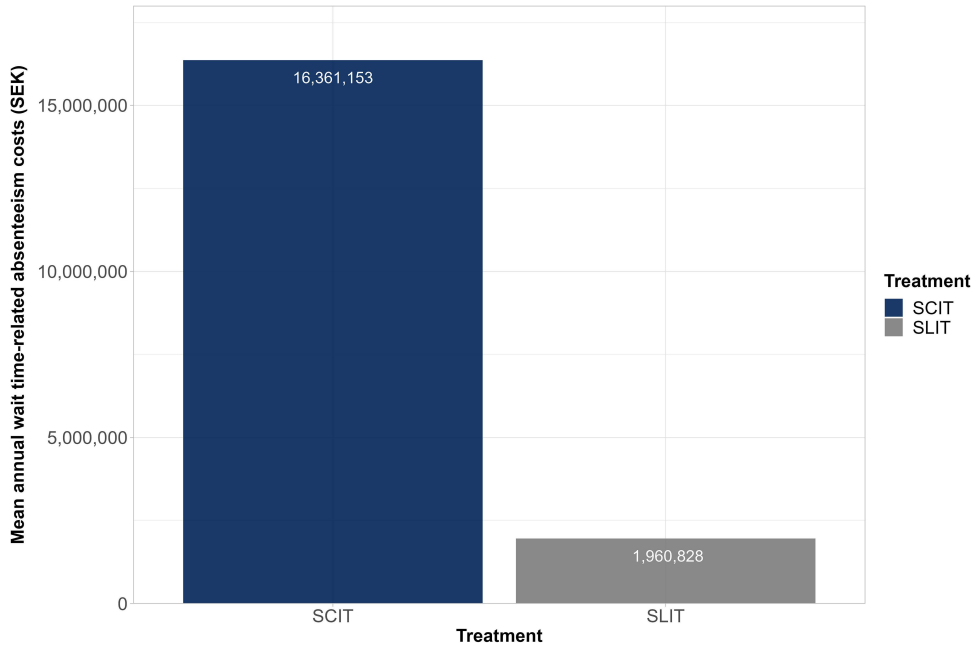

Figure 6 Mean total annual waiting time-related absenteeism.
Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

absenteeism (3.0%). Private transport contributed the least to overall costs (1.4%). A summary of cost contributions per category can be found in Figure 1.

For each patient receiving SLIT tablets, mean total costs amounted to SEK 45,000. Medication contributed the most to these costs (79.8%), followed by clinical appointments (16.7%), travel-related absenteeism (2.9%) and private transport costs (0.4%). Waiting time-related absenteeism contributed the least to overall costs (0.2%). Again, a summary of cost contributions per category can be found in Figure 1.

Appointment Costs

For each patient receiving SCIT, mean total appointment costs were SEK 57,300. Of the SEK 57,300, SEK 3900 comprised direct costs for the patient, with the remaining SEK 53,400 comprising government reimbursements.

For each patient receiving SLIT tablets, mean total appointment costs were SEK 7500, 7.64 times lower than SCIT appointment costs. Again, SEK 3900 comprised direct costs for the patient, with the remaining SEK 3600 comprising government reimbursements.

Medication Costs

For each patient receiving SCIT, mean total medication costs were SEK 26,800, with 100% of this cost burden again falling solely on specialized AR treatment centers.

For each patient receiving SLIT tablets, mean total medication costs were SEK 35,900, 1.34 times higher than SCIT medication costs. Of the SEK 35,900, SEK 7800 comprised direct costs for the patient cost, with the remaining SEK 28,100 comprising government reimbursements.

Private Transport Costs

For each patient receiving SCIT, mean total private transport costs were SEK 1400 (SD: SEK 311), 99% of which arose from private cars. For each patient receiving SLIT tablets, mean total private transport costs were SEK 187.9 (SD: SEK 40.8), 7.45 times lower than SCIT private transport costs). Of the SEK 187.9, SEK 186.2 arose from private cars.

Travel-Related Absenteeism

For each SCIT patient, mean total travel-related absenteeism costs were SEK 9600 (SD: SEK 2100), with SEK 7600 arising from private car travel. For each patient receiving SLIT tablets, mean total travel-related absenteeism costs were SEK 1300 (SD: SEK 274), 7.38 times lower than SCIT travel-related absenteeism costs). Of the SEK 1300, SEK 994 arose from private car travel.

Waiting Time-Related Absenteeism

For each patient receiving SCIT, mean total waiting time-related absenteeism costs were SEK 2900. For each patient receiving SLIT tablets, mean total waiting time-related absenteeism costs were SEK 96.5, 30.05 times lower than SCIT waiting time-related absenteeism costs.

Discussion

The present study sought to determine the cost of SCIT and SLIT-tablets for patients with moderate-severe AR in Sweden. Specifically, investigations surrounding the direct and indirect costs arising from the impacts of patient travel were conducted, based on the results from Cardell and Sterner et al.[17] Treatment-related travel burdens and indeed treatment-related CO_2 emissions are now starting to be investigated in the wider literature, with a focus placed both on specific treatments[38] and healthcare treatment/systems in general.[19,39] However, to our knowledge, this is the first study that seeks to comprehensively determine the financial burdens associated with treatment-related travel and to explore the impact of CO_2 emissions (discussed below).

The analysis determined that for most cost categories SLIT-tablets resulted in significant savings relative to SCIT. Specifically, for the modelled one-year snapshot cohort of 20,330 moderate-severe AR patients, SCIT was associated with the following: SEK 318.6m in appointment costs, SEK 8m in private transport costs, SEK 53.6m in travel-related absenteeism, and SEK 16.4m in waiting time-related absenteeism. Comparatively, SLIT-tablets were associated with the following: SEK 76.4m in appointment costs, SEK 1.9m in private transport costs, SEK 12.8m in travel-related absenteeism, and SEK 2.0m in waiting time-related absenteeism. Even when considering that medication costs for SLIT-tablets (SEK 243.1m) were higher than those for SCIT (SEK 207.5m), overall, SLIT-tablets would result in SEK 267.9m in savings. Results for the three-year incident cohort followed a similar pattern, with SLIT-tablets associated with SEK 53,000 in savings per patient, relative to SCIT. When using the calculated cost-per-hour figure of SEK 334.2 for the sensitivity analysis, travel-related absenteeism and waiting time-related absenteeism costs were both significantly higher than those in the base case (Table 3). These trends correlate with the published literature, which suggest that globally, high medication

Table 2 Summary of Mean Costs per Category for One-Year and Three-Year Cohorts

Cost Category	SLIT-Tablets	SCIT	Additional Costs for SCIT
One-year cohort (costs in million SEK)			
Appointments	76.4	318.6	+242.2
Medication	243.1	207.5	−35.6
Private transport	1.9	8.0	+6.1
Travel-related absenteeism	12.8	53.6	+40.8
Waiting time-related absenteeism	2.0	16.4	+14.4
Total	**336.2**	**604.1**	**267.9**
Three-year cohort (costs in thousand SEK)			
Appointments	7.5	57.3	+49.8
Medication	35.9	26.8	−9.1
Private transport	0.2	1.4	+1.2
Travel-related absenteeism	1.3	9.6	+8.3
Waiting time-related absenteeism	0.1	2.9	+2.8
Total	**45.0**	**98.0**	**53.0**

Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

Table 3 Results Comparison: Base Case and Sensitivity Analyses

Cost Category	SLIT-Tablets	SCIT
One-year cohort (costs in million SEK)		
Base case (cost-per-hour SEK 192.90)		
Travel-related absenteeism	12.8	53.6
Waiting time-related absenteeism	2.0	16.4
Sensitivity analysis (cost-per-hour SEK 334.2)		
Travel-related absenteeism	22.2	92.8
Waiting time-related absenteeism	3.4	28.3
Three-year cohort (costs in thousand SEK)		
Base case (cost-per-hour SEK 192.90)		
Travel-related absenteeism	1.3	9.6
Waiting time-related absenteeism	0.1	2.9
Sensitivity analysis (cost-per-hour SEK 334.2)		
Travel-related absenteeism	2.2	16.7
Waiting time-related absenteeism	0.2	5.1

Abbreviations: SCIT, subcutaneous immunotherapy; SEK, Swedish Krona; SLIT, sublingual immunotherapy.

costs in particular are a source of strain on public healthcare budgets and wider resource allocation.[40] A full breakdown and comparison of costs per category for both the one-year and three-year cohorts can be found in Table 2.

Another cost to be considered but not yet discussed is the social cost of carbon, a commonly applied measure used to estimate the expected damages resulting from CO_2 emissions or their equivalent.[41] Some current estimates for the social cost of CO_2 include United States Dollars (USD) 185/ton,[42] EUR 100.17/ton,[43] and USD 51/ton.[44] For the one-year cohort, total mean annual CO_2 emissions were estimated to be approximately 1700 tons for SCIT, and approximately 410 tons for SLIT-tablets, based on results from the original travel algorithm. According to the three estimates for the social cost of CO_2, SLIT tablets could therefore be associated with annual savings of either USD 238,650, EUR 129,219, or USD 65,790. These savings, in addition to the direct and indirect cost savings outlined in the results, demonstrate that moderate-severe AR patients, the healthcare system, and wider society can benefit from SLIT-tablets being used instead of SCIT in Sweden. It is important, however, to acknowledge that carbon tax would likely already be reflected within the private transport costs estimated as part of the present analysis (ie, the tax would likely be incorporated within payments made by patients when purchasing petrol for their private transport vehicle). Therefore, at least some proportion of the potential social costs of CO_2 presented above would be offset by the carbon tax already incorporated within the model.

The strengths and weaknesses associated with the original travel algorithm model, as well as various assumptions related to treatment- and travel, can be found in Cardell and Sterner et al[17] and will therefore not be discussed here. However, there were a number of strengths associated with the methodology and inputs used to determine costs. Firstly, the use of robust data sources from Swedish institutions to determine costs for appointments, as well as hourly pay for absenteeism, mean that the final results are likely to be a valid representation of the costs experienced by moderate-severe AR patients, healthcare systems, and employers. The incorporation of the high-cost protection scheme for outpatient appointments and high-cost reimbursement scheme for medication prescriptions meant that patient costs for these aspects were accurately represented. Furthermore, a high level of detail was therefore considered when presenting said costs, by determining how various financial burdens associated with SCIT and SLIT-tablets would be shared by relevant payers.

A second strength was determining a wide range of costs for SCIT and SLIT-tablets (both direct and indirect) associated with treatment, treatment waiting times, treatment-related travel and wider societal costs due to carbon emissions. It is important to note that there are further implications for each of these costs that may even be considered partially positive (eg, higher private transport costs could mean higher fuel tax revenues for governments, which are likely to be re-invested on public services such as healthcare and transport).[45,46] However, the flow of healthcare-related funds across various stakeholders in Sweden can be incredibly complex, and whilst they can provide additional context to the weight and future impacts of treatment-related costs, they were not explored as part of this study.

The study also used a conservative official figure (SEK 192.90) for hourly pay in order to determine absenteeism costs. The alternative cost-per-hour figure of SEK 334.2 however, demonstrates that a comprehensive and widely representative hourly pay associated with actual time spent working could be higher than the base case figure presented, which would drive absenteeism costs up further (see Table 3). These factors mean that the results presented here may represent an underestimate of the true financial benefits of SLIT-tablet therapy, especially when considering that absenteeism costs were significantly higher for SCIT. Additionally, the model also did not account for the fact that SLIT appointments (particularly follow-ups) could also take place with the patient's local general practitioner (GP). This factor would yield reduced treatment-related travel and appointment costs (as GP appointments are typically cheaper than those with an allergy specialist within an AR treatment center[47]) associated with SLIT-tablets even further.

One limitation of the study is that whilst the high-cost protection scheme was applied for outpatient appointments, an aspect not considered was the region-specific maximum cap that patients pay on a per-appointment basis (ie, patient fees).[48] Although incorporating these caps would be relevant and allow for a more region-specific analysis with regard to appointment costs, publicly available data for these regional costs were not available and would likely have been too complex to implement accurately within the model. Moreover, regional-specific differences in said costs would be unlikely to have a significant impact on the final results.

The model did not account for public transport costs, as it would be difficult to accurately determine how the financial burden of each cost type would be distributed across stakeholders. Other omitted travel-related costs included road vehicle tax, wear and tear to public infrastructure, congestion tax and road tax. The reason for these omissions was rooted

in the challenges in identifying suitable data sources, as well as the intricate complexities associated with applying said data sources in a relevant and reliable manner, without double-counting the same costs elsewhere. Finally, no associated wait-time and subsequent absenteeism cost was determined for patients attending their second appointment for SLIT-tablet therapy (ie, the simple follow-up). In routine practice, there would likely be a specific "consultation time" and related absenteeism cost associated with the follow-up appointment which would vary from patient to patient. However, we were unable to identify a data source that reliably determined mean consultation time. Although this omission could suggest that the results may overestimate the cost-savings associated with SLIT-tablet therapy, the limited number of follow-up appointments and their anticipated short-time duration would be unlikely to significantly impact the results. Another omission from the model was the presenteeism costs associated with each therapy. Whilst assumed that due to their similar clinical efficacy both treatments would have comparative presenteeism costs, results from a recent study suggest that SLIT may actually possess further cost savings associated with this productivity loss category, based on current timelines for treatment initiation.[49] Indeed, this would suggest that the results presented here possess an additional level of conservatism with regard to societal cost savings associated with SLIT tablets. A final limitation is that the model assumed that all patients would receive either SCIT or SLIT-tablets. In routine practice however, not all patients receiving SCIT are able to be transferred to SLIT-tablet therapy. This is due to the fact that SCIT can be used for a comparatively wider range of allergens than SLIT tablets.

Conclusion

For patients with moderate-severe AR receiving AIT in Sweden, SLIT-tablets demonstrated significant potential cost savings in terms of appointments, private travel, and absenteeism relative to SCIT injections. Switching patients receiving SCIT to SLIT-tablets could alleviate financial burdens on patients, the healthcare system and the government, whilst reducing the burden of treatment-related CO_2 emissions on society.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Acknowledgment

Lars-Olaf Cardell and Thomas Sterner share first authorship.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

RFP is a full-time employee, director, and shareholder of Covalence Research Ltd, and WA is a full-time employee of, Covalence Research Ltd, which received consultancy fees from ALK to develop the transportation and CO_2 emissions algorithm, run the analysis and prepare the manuscript. AK and MS are current employees of ALK. LOC has received institutional grants and/or personal fees from Orion Pharma, Sanofi, GlaxoSmithKline and ALK-Abello. TS has no competing interests to declare.

References

1. Holmström M, Davidsson Å, Stridh B, et al. Allergisk rinit hos barn och vuxna [Allergic rhinitis in children and adults - international recommendations adapted to the clinical situation in Sweden]. *Lakartidningen*. 2023;120:23041. Swedish.
2. Small P, Keith PK, Kim H. Allergic rhinitis. *Allergy Asthma Clin Immunol*. 2018;14(S2):51. doi:10.1186/s13223-018-0280-7
3. Varshney J, Varshney H. Allergic rhinitis: an overview. *Indian J Otolaryngol Head Neck Surg*. 2015;67(2):143–149. doi:10.1007/s12070-015-0828-5
4. Tkacz JP, Rance K, Waddell D, et al. Real-world evidence costs of allergic rhinitis and allergy immunotherapy in the commercially insured United States population. *Curr Med Res Opin*. 2021;37(6):957–965. doi:10.1080/03007995.2021.1903848

5. Kremer B, Den Hartog HM, Jolles J. Relationship between allergic rhinitis, disturbed cognitive functions and psychological well-being. *Clin Exp Allergy*. 2002;32(9):1310–1315. doi:10.1046/j.1365-2745.2002.01483.x
6. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008;63(Suppl 86):8–160. doi:10.1111/j.1398-9995.2007.01620.x
7. Greiner AN, Hellings PW, Rotiroti G, et al. Allergic rhinitis. *Lancet*. 2011;378(9809):2112–2122. doi:10.1016/S0140-6736(11)60130-X
8. Bousquet J, Neukirch F, Bousquet PJ, et al. Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol*. 2006;117(1):158–162. doi:10.1016/j.jaci.2005.09.047
9. Eriksson J, Ekerljung L, Rönmark E, et al. Update of prevalence of self-reported allergic rhinitis and chronic nasal symptoms among adults in Sweden. *Clin Respir J*. 2012;6(3):159–168. doi:10.1111/j.1752-699X.2011.00269.x
10. Cardell L-O, Olsson P, Andersson M, et al. TOTALL: high cost of allergic rhinitis-a national Swedish population-based questionnaire study. *NPJ Prim Care Respir Med*. 2016;26(1):15082. doi:10.1038/npjpcrm.2015.82
11. Hellgren J, Cervin A, Nordling S, et al. Allergic rhinitis and the common cold - high cost to society. *Allergy*. 2010;65(6):776–783. doi:10.1111/j.1398-9995.2009.02269.x
12. Sur DKC, Plesa ML. Treatment of allergic rhinitis. *Am Fam Physician*. 2015;92(11):985–992.
13. Varney VA, Gaga M, Frew AJ, et al. Usefulness of immunotherapy in patients with severe summer hay fever uncontrolled by antiallergic drugs. *BMJ*. 1991;302(6771):265–269. doi:10.1136/bmj.302.6771.265
14. Sánchez-Borges M, Bernstein DI, Calabria C. Subcutaneous immunotherapy safety: incidence per surveys and risk factors. *Immunol Allergy Clin North Am*. 2020;40(1):25–39. doi:10.1016/j.iac.2019.09.001
15. Dretzke J, Meadows A, Novielli N, et al. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. *J Allergy Clin Immunol*. 2013;131(5):1361–1366. doi:10.1016/j.jaci.2013.02.013
16. Saporta D. Efficacy of sublingual immunotherapy versus subcutaneous injection immunotherapy in allergic patients. *J Environ Public Health*. 2012;2012:492405. doi:10.1155/2012/492405
17. Cardell L-O, Sterner T, Ahmed W, et al. Modelling the impact of sublingual immunotherapy versus subcutaneous immunotherapy on patient travel time and CO2 emissions in Sweden. *Sci Rep*. 2024;14(1):1575. doi:10.1038/s41598-024-51925-8
18. Ali F. NICE's strategy on sustainability: current progress and next steps. NICE; 2020. Available from: https://www.nice.org.uk/news/blog/current-progress-and-next-steps-on-sustainability. Accessed May 31, 2024.
19. Lenzen M, Malik A, Li M, et al. The environmental footprint of health care: a global assessment. *Lancet Planet Health*. 2020;4(7):e271–e279. doi:10.1016/S2542-5196(20)30121-2
20. Wallskär H. Fler får immunterapi mot allergier. LäkemedelsVärlden; 2022. Available from: https://www.lakemedelsvarlden.se/immunterapi-mot-allergier-okar/. Accessed May 31, 2024.
21. emc. ITULAZAX 12 SQ-Bet - Summary of Product Characteristics (SmPC); 2022. Available from: https://www.medicines.org.uk/emc/product/12906. Accessed May 31, 2024.
22. FASS. Alutard SQ 5-Grass. fass.se; 2021. Available from: https://www.fass.se/LIF/product?userType=2&nplId=19901102000807. Accessed May 31, 2024.
23. Pollock RF, Slættanes AK, Brandi H, et al. A cost-utility analysis of SQ® Tree SLIT-tablet versus placebo in the treatment of birch pollen allergic rhinitis from a Swedish societal perspective. *Clin Outcomes Res CEOR*. 2023;15:69–86.
24. 1177.se. Högkostnadsskydd för öppenvård. 1177. Available from: https://www.1177.se/sa-fungerar-varden/kostnader-och-ersattningar/hogkostnadsskydd-for-oppenvard/. Accessed May 31, 2024.
25. FASS. Itulazax. fass.se; 2022. Available from: https://www.fass.se/LIF/product?userType=2&nplId=20180727000034. Accessed May 31, 2024.
26. E-hälsomyndigheten. Raised limits in the high-cost reimbursement scheme on January 1st 2023; 2022. Available from: https://www.ehalsomyndigheten.se/languages/english/raised-limits-in-The-high-cost-reimbursement–scheme-on-january-1st-2023/.
27. Buy Alutard SQ Birch suspension for injection strength series, 4 x 5 milliliters | apoteket.se. Available from: https://www.apoteket.se/produkt/alutard-sq-bjork-injektionsvatska-suspension-styrkeserie-4-x-5-milliliter-kombinationsforpackning-52520/. Accessed May 31, 2024.
28. Buy Alutard SQ Birch, inj-liquid, suspension 100,000 SQ-E/mL, 5 milliliters | apoteket.se. Available from: https://www.apoteket.se/produkt/alutard-sq-bjork-injektionsvatska-suspension-100-000-sq-e-per-mL-5-milliliter-injektionsflaska-52519/. Accessed May 31, 2024.
29. Energimyndigheten. Energiläget. Available from: https://www.energimyndigheten.se/statistik/energilaget/?currentTab=1. Accessed May 31, 2024.
30. International Energy Agency. Fuel economy in major car markets: technology and policy drivers 2005-2017. Paris: International Energy Agency; 2019. Available from: https://www.iea.org/reports/fuel-economy-in-major-car-markets. Accessed May 31, 2024.
31. Koopmanschap MA, Rutten FF. Indirect costs in economic studies: confronting the confusion. *PharmacoEconomics*. 1993;4(6):446–454. doi:10.2165/00019053-199304060-00006
32. Drummond MF, Sculpher MJ, Claxton K, et al. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford University Press; 2015.
33. Gosselin E, Lemyre L, Corneil W. Presenteeism and absenteeism: differentiated understanding of related phenomena. *J Occup Health Psychol*. 2013;18(1):75–86. doi:10.1037/a0030932
34. Average hourly earnings, including overtime pay, of manual workers in the private sector, time series. Stat. Cent. Available from: https://www.scb.se/en/finding-statistics/statistics-by-subject-area/labour-market/wages-salaries-and-labour-costs/short-term-statistics-wages-and-salaries-private-sector-klp/pong/tables-and-graphs/manual-workers/average-hourly-earnings-including-overtime-pay-of-manual-workers-in-The-private-sector-time-series/. Accessed May 31, 2024.
35. Medlingsinstitutet. Lönestrukturstatistik. Medlingsinstitutet; 2019. Available from: https://www.mi.se/lonestatistik/lonestrukturstatistik/. Accessed May 31, 2024.
36. SCB. Medelarbetstid (faktisk) per vecka för sysselsatta 15-74 år (AKU) efter anknytningsgrad till arbetsmarknaden, kön och ålder. År 2021 - 2022. Statistikdatabasen. Available from: http://www.statistikdatabasen.scb.se/pxweb/sv/ssd/START__AM__AM0401__AM0401S/NAKUFaktMedArbtidAr/. Accessed May 31, 2024.
37. Regeringen och Regeringskansliet. Annual Leave Act (Semesterlagen). Regeringskansliet. Regeringen och Regeringskansliet; 2016. Available from: https://www.government.se/government-policy/labour-law-and-work-environment/1977480-annual-leave-act-semesterlagen/. Accessed May 31, 2024.
38. Coombs NJ, Coombs JM, Vaidya UJ, et al. Environmental and social benefits of the targeted intraoperative radiotherapy for breast cancer: data from UK TARGIT-A trial centres and two UK NHS hospitals offering TARGIT IORT. *BMJ Open*. 2016;6(5):e010703. doi:10.1136/bmjopen-2015-010703

39. Andrews E, Pearson D, Kelly C, et al. Carbon footprint of patient journeys through primary care: a mixed methods approach. *Br J Gen Pract*. 2013;63(614):e595–603. doi:10.3399/bjgp13X671579
40. Vincent Rajkumar S. The high cost of prescription drugs: causes and solutions. *Blood Cancer J*. 2020;10(6):71. doi:10.1038/s41408-020-0338-x
41. Ricke K, Drouet L, Caldeira K, et al. Country-level social cost of carbon. *Nat Clim Change*. 2018;8(10):895–900. doi:10.1038/s41558-018-0282-y
42. Rennert K, Errickson F, Prest BC, et al. Comprehensive evidence implies a higher social cost of CO2. *Nature*. 2022;610(7933):687–692. doi:10.1038/s41586-022-05224-9
43. Hodgson C, Sheppard D EU carbon price tops €100 a tonne for first time. Financ Times; 2023. Available from: https://www.ft.com/content/7a0dd553-fa5b-4a58-81d1-e500f8ce3d2a. Accessed May 31, 2024.
44. Rennert K, Prest BC, Pizer WA, et al. The social cost of carbon: advances in long-term probabilistic projections of population, GDP, emissions, and discount rates. Brookings; 2021. Available from: https://www.brookings.edu/articles/the-social-cost-of-carbon/. Accessed May 31, 2024.
45. Anell A, Glenngård AH, Merkur S. Sweden health system review. *Health Syst Transit*. 2012;14:1–159.
46. Regeringskansliet R. Central government budget in figures. Regeringskansliet. Regeringen och Regeringskansliet; 2019. Available from: https://www.government.se/government-of-sweden/ministry-of-finance/central-government-budget/central-government-budget-in-figures/. Accessed May 31, 2024.
47. Department of Health and Social Care, Foreign & Commonwealth Office, Foreign, Commonwealth & Development Office. Healthcare for UK nationals living in Sweden. GOV.UK; 2021. Available from: https://www.gov.uk/guidance/healthcare-in-sweden. Accessed May 31, 2024.
48. Öster K. Patientavgifter och högkostnadsskydd. 1177.se; 2023. Available from: https://www.1177.se/sa-fungerar-varden/kostnader-och-ersattningar/patientavgifter/. Accessed May 31, 2024.
49. Olsson P, Skröder C, Ahlbeck L, et al. HealthSWEDE: costs with sublingual immunotherapy—a Swedish questionnaire study. *Allergy Asthma Clin Immunol*. 2021;17(1):55. doi:10.1186/s13223-021-00560-3