

Cost of allergy immunotherapy: sublingual vs subcutaneous administration

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Background: Allergy immunotherapy is an effective way to manage the allergic patient and may be administered either through the subcutaneous route (SCIT) or the sublingual route (SLIT). Both have been proven efficacious; however, SLIT is currently not covered by insurance companies and is an out-of-pocket expense. The goal of the current study is to compare the costs of SCIT to SLIT.

Methods: For SCIT, a total of 9 different insurance groups were studied including 8 preferred provider organizations (PPOs) and Medicare. Costs were broken down according to the percentage of coverage for the injections, serum vial fees, weekly co-pay, and deductibles. Total yearly cost for SCIT was calculated for the varying insurance plans and compared to the yearly cost of SLIT.

Results: PPO plans covered between 60% and 100% of allergy immunotherapy treatment with a range of weekly co-pay between \$0 and \$50. Deductibles ranged between \$0 and \$7000. Medicare had a flat rate of 80% coverage costing the insurer \$807.20 for the year of therapy. None of the above costs include loss of work productivity and travel expense. The cost of SLIT ranged from \$500 to \$2100 de-

pending on the allergy practice and number on antigens treated.

Conclusion: The cost of SCIT varies dramatically according to insurance plan whereas the cost of SLIT varies between practices. When loss of productivity and travel expense are added into the cost of SCIT, SLIT might be comparable in cost and more convenient for the patient. Although the lack of insurance coverage for SLIT currently makes it more expensive than SCIT, we have found that the financial gap is much smaller than initially thought, especially when indirect costs and plans with less than 80% coverage or high weekly co-pay are factored into the equation. © 2012 ARS-AAOA, LLC.

Key Words:

subcutaneous immunotherapy; sublingual immunotherapy; cost; insurance coverage; allergy; allergic rhinitis; perennial allergies

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Allergy immunotherapy is a valid treatment option in patients with seasonal or perennial allergies who have failed medical therapy. Immunotherapy may be administered either through the traditional subcutaneous route (SCIT) or more recently through a sublingual route (SLIT), which allows specific antigens placed under the tongue to induce tolerance. The majority of injections for SCIT are

given under direct supervision in an office setting whereas SLIT, for the most part, is done at home. SLIT is considered a viable alternative to injection (SCIT) therapy and is endorsed by the World Health Organization.¹ Clinical trials have demonstrated that SLIT is an effective and safe treatment.² The effects of SLIT appear to be long-lasting, with studies showing continued efficacy 4 to 5 years after discontinuing therapy.³ In addition, SLIT appears to have less risk of systemic side effects and anaphylaxis. SLIT is well tolerated, with side effects ranging from oral itching and swelling to gastrointestinal symptoms (nausea, vomiting, diarrhea, and stomach ache). Most side effects are mild and self-limiting.⁴ The SLIT Joint Task Force reviewed data on 1,181,654 doses administered to 4378 patients and found no fatalities with an estimated systemic reaction of 0.056%, which included asthma, urticaria, and gastrointestinal symptoms.⁵ This is in comparison to the systemic reaction rate to nonaccelerated SCIT, which ranges from 0.05% to 3.2% of injections.

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TABLE 1. Demonstration of how the cost of SLIT that is charged to the patient may change according to the volume of antigen used to mix the vials*

Amount of allergen added	10 allergens (\$)	15 allergens (\$)	20 allergens (\$)	25 allergens (\$)
0.6 mL	960	1140	1320	1500
1.0 mL	1200	1500	1800	2100

*The prices depicted are from a single tertiary-care allergy practice and include practice costs such as overhead and liability coverage. The dollar amount above reflects the total cost to the patient for 1 year of SLIT.

SLIT = sublingual allergy immunotherapy.

Although not Food and Drug Administration (FDA)-approved in the United States, SLIT is frequently used in an off-label manner to treat inhalant allergies. Therefore, at this time insurance companies do not cover SLIT and it is considered an out-of-pocket expense for those who wish to seek the convenience of this treatment. SLIT is attractive to many patients because it is tolerable, safe, and convenient, and for the most part is done at home. It is an attractive option for young children who are opposed to injections. However, many patients are deterred due to the high out-of-pocket cost of SLIT. The cost of SLIT is determined by the number and volume of antigens added to a 10-mL treatment. The volume of antigen added to a 10-mL vial typically ranges from 0.4 to 1.0 mL. This range in antigen volume can significantly affect the price of SLIT, as demonstrated in Table 1. In addition, the final price of SLIT may include practice costs such as overhead and liability coverage. Thus, the cost of SLIT may vary significantly across practices. The cost of SCIT, on the other hand, depends on the type of insurance plan, percentage of coverage for the injections and serum vials, weekly co-pay amount, and deductible that has to be met. In addition, time, loss of work productivity, and travel expense add to the cost of SCIT. Therefore, depending on an individual's insurance plan and calculated cost for travel and loss of work expense, SLIT may be comparable or even more cost effective than SCIT.

Several studies have looked at the cost savings of SCIT and SLIT compared to standard medical therapy.⁶⁻⁹ However, only 1 study to date from Europe has directly compared the cost savings of SCIT to SLIT.¹⁰ The goal of this study is to compare the cost of SCIT according to various insurance coverage plans in the United States with the cost of SLIT.

Methods

Nine different insurance groups were studied including 8 preferred provider organizations (PPOs) and Medicare. Cost of SCIT was broken down according to the percentage of coverage for the injections, serum vial fees, weekly co-pays, and plan deductibles. Several different allergy practices across the United States were contacted and asked to divulge the amount they charge to their patients for SLIT.

TABLE 2. Yearly cost and weekly co-pays that may be incurred with visits for SCIT*

Typical weekly co-pay for allergy injection visits (\$)	Total yearly cost of weekly allergy injection visits (\$)
0.00	0.00
5.00	260.00
10.00	520.00
15.00	780.00
20.00	1040.00
25.00	1300.00
30.00	1560.00
40.00	2080.00
50.00	2600.00

*Eight PPOs were studied; each row represents data from 1 PPO. The price does not include cost of serum vial, injection fee, or deductible.

SCIT = subcutaneous allergy immunotherapy.

Results are reported as what the final charges to the patient would be according to the number of antigens treated. No attempt was made to determine the cost of SLIT according to the volume of antigen used, as this is not uniform between practices. Total yearly costs for SCIT were calculated for the varying insurance plans and compared to SLIT.

Results

PPO plans covered between 60% and 100% of allergy immunotherapy, with a weekly co-pay range between \$0 and \$50. The total yearly cost of just the weekly co-pay is shown in Table 2. Between the 8 PPO insurance companies studied, the deductibles varied according to plan and ranged between \$0 and \$7000. The average yearly cost of immunotherapy is calculated by combining the weekly co-pay, weekly injection fee, and serum vial fee. The weekly injection fee and serum vial fee vary according to each individual insurance plan (Table 3). Table 4 depicts the total cost of immunotherapy with and without the cost of the deductible. Medicare has a flat rate of 80% coverage, costing the insurer \$807 for the year of therapy. None of the above costs include loss of work productivity and travel expenses. There is no uniform cost of SLIT, which varies widely across practices even within the same region. We contacted 15 allergy practices across the United States that offer SLIT to their patients. Thirteen of those 10 practices revealed what the average yearly charges are for patients undergoing SLIT (Table 5). The practices differed in terms of cost, with some charging flat rates despite the number on antigens used while others charged per antigen used. Some practices offered SLIT up to 25 antigens while others only offered SLIT up to 10 antigens. Those offering SLIT only up to 10 antigens had a significantly reduced cost. The results show a significant disparity in cost, which may be related to the variability in the volume of antigen used to

TABLE 3. Charges to the patient for 1 year of SCIT based on percentage of insurance coverage*

Insurance coverage (%)	Multiple-injection fees/year (\$)	Single-injection fees/year (\$)	Serum vial fee/year (\$)
100	0.00	0.00	0.00
95	111.80	75.40	90.00
90	223.60	150.00	180.00
85	335.40	226.20	270.00
80	447.20	301.60	360.00
70	670.80	452.40	540.00
65	782.60	527.80	630.00
60	894.40	603.20	720.00
Pay out of pocket	2236.00	1508.00	1800.00

*The prices of the injection and serum vial fee vary based on insurance coverage. Prices will differ for multiple-injection fees, which includes patients being treated for more than 13 antigens, and single-injection fees, which includes patients being treated for <13 antigens.

^aSerum vial fee for 1 vial, which can hold up to 13 antigens and 10 doses. SCIT = subcutaneous allergy immunotherapy.

mix the SLIT vials, as demonstrated in Table 1. A generalized cost comparison between SCIT and SLIT is difficult to perform due to multiple factors that influence cost between both treatment options. However, in Table 6, we give 4 hypothetical examples of what SCIT would cost compared to SLIT.

Discussion

The therapeutic benefit of both SLIT and SCIT has been widely endorsed by allergists nationwide. Currently, the majority of the data regarding SLIT therapy originates from Europe, where SLIT is seen as the standard of care. The phi-

TABLE 5. Cost of SLIT according to allergy practice and antigens mixed into the SLIT vial

Allergy practice	≤10 antigens	15 antigens	20 antigens	25 antigens
1	950	1100	1250	1500
2	1200	1500	1800	2100
3	960	1140	1300	1500
4	1000	1200	1500	1500
5	1000	1100	1150	1200
6 ^a	600			
7 ^b	1000	1000	1000	
8	500	1000	1300	1420
9 ^b	900	900	900	
10	1000	1000	1200	1200
11 ^c	700	700		
12 ^a	540			
13 ^a	900			

^aPractice only offers SLIT up to 10 antigens.

^bPractice only offers SLIT up to 20 antigens.

^cPractice only offers SLIT up to 15 antigens.

SLIT = sublingual allergy immunotherapy.

losophy of SLIT in Europe also differs slightly from that in the United States. In Europe, typically only select allergens are chosen for therapy whereas in the United States, the trend is to treat with most if not all the allergens a for which a patient tests positive. This has significant implications when comparing data between U.S. and European studies, as the cost of SLIT has the potential to vary greatly depending on the number of antigens used in therapy. Finally, the model of health care in European countries is

TABLE 4. Total yearly costs for SCIT incurred by the patient based on the coverage offered by 9 different insurance policies

Insurance	Coverage (range,%)	Weekly co-pay (range, \$)	Deductible (range, \$)	Average yearly cost excluding deductible (\$)	Average yearly cost with deductible (\$)	Total yearly cost with deductible (range, \$)	Total yearly cost excluding deductible (range, \$)
1	80.00-100.00	0.00-50.00	0.00-2500.00	1174.00	1841.00	520.00-5100.00	520.00-2600.00
2	80.00-100.00	0.00-5.00	0.00-600.00	360.40	597.90	0.00-1407.00	0.00-807.00
3	80.00-100.00	0.00-40.00	0.00-2500.00	628.40	926.40	0.00-2903.00	403.60-2080.00
4	80.00-100.00	0.00-30.00	0.00-6000.00	533.10	2052.40	0.00-6000.00	0.00-1847.20
5	70.00-100.00	0.00-40.00	0.00-5000.00	726.80	1062.70	0.00-6210.00	0.00-2080.00
6	70.00-100.00	0.00-35.00	0.00-3000.00	582.40	946.40	0.00-4210.00	0.00-1820.00
7	60.00-100.00	0.00-50.00	0.00-7000.00	720.20	1364.50	0.00-6040.00	0.00-2887.20
8	70.00-100.00	0.00	200.00-1250.00	403.60	970.30	200.00-2460.00	0.00-1210.80
Medicare	80.00	0.00	0.00	807.20	807.20	807.20	807.20

*Costs include fee for the serum vial, multiple injection fee, weekly co-pay, and deductible. Insurance companies 1 through 8 represent the most common PPO plans in Southern California.

PPO = preferred provider organization; SCIT = subcutaneous allergy immunotherapy.

TABLE 6. Cost of SCIT vs SLIT for treatment of 15 allergens with several insurance options

Insurance coverage	SCIT (\$) ^a	SLIT 15 antigens (\$) ^b
90%/\$30 co-pay	2143.60	700.00-1500.00
80%/\$0 co-pay	1167.20	700.00-1500.00
80%/\$20 co-pay	2207.20	700.00-1500.00
90%/10 co-pay	1103.60	700.00-1500.00
Medicare 80%/no co-pay	1167.20	700.00-1500.00

^aSCIT therapy for 15 allergens requires the cost of 2 serum vials because 1 vial can only hold 13 allergens.

^bThe range in the cost of SLIT for 15 antigens as determined by the results in Table 5.

SCIT = subcutaneous allergy immunotherapy; SLIT = sublingual allergy immunotherapy.

predominantly some form of universal health coverage, which is a drastic difference from the private insurer model that dominates healthcare in the United States. As such, numbers comparing cost of immunotherapy for both SCIT and SLIT between Europe and the United States can only be approximations.

The goal of this study was to compare the direct medical costs of SLIT vs SCIT. For SLIT this cost was dependent on the number of antigens used to treat the patient plus additional costs, including overhead, liability, and profit margin. The model of compensation used in this study is that of a multispecialty practice at a tertiary referral center at a major medical university. The average cost of SLIT at this institution varies between \$960 and \$2100 dollars annually, paid in totality before initiating therapy. However, wide ranges in compensation models exist in other university practices as well as private practices, as shown in Table 5. Because SLIT is not covered by insurance in the United States, the decision on how to charge is based purely on the prerogative of the practice. Through conversations at the annual meeting of the American Academy of Otolaryngic Allergy as well as discussions with patients transferring their care from other practices, annual rates as low as \$500 to as high as \$5000 have been quoted. Of note, the prices at the lower end of the spectrum often are for much lower volume and number of antigens included in the treatment protocol.

The direct medical cost for SCIT is even more complicated because of the wide range of insurance coverage in the United States. Often, coverage will vary even within a specific insurance company depending on the exact plan purchased by the patient or the patient's employer. This is further complicated by the fact that many older patients will have a private policy that typically covers 20% of medical costs incurred, in addition to government-sponsored Medicare.

When analyzing the cost of SCIT, patients will generally need to pay a percentage of the weekly injection fee as well as a percentage of all serum vials, which are mixed on average every 10 to 12 weeks. In addition a co-pay

may be collected with each visit and many plans require a deductible to be met before covering for SCIT. Depending on the specific plan purchased, a deductible can range from several hundred dollars to more than \$5000.

If one should be so fortunate as to have a healthcare plan in the United States that covers 100% of healthcare costs, the financial distinction between SCIT and SLIT becomes obvious. It can be seen very quickly that the majority of patients in the United States are not so fortunate and in fact often present with a coverage plan which involves a significant deductible and/or a high percentage of out-of-pocket expenses. When factoring in the cost of weekly injections for several years, as well as the accumulated expenses of mixing treatment vials, costs begin to accrue very rapidly even with the patient paying only 10% of expenses. When a patient becomes responsible for 20% and higher, the cost of SCIT rapidly begins to approach that of the out-of-pocket fees for SLIT. As immunotherapy typically requires weekly visits to the allergy clinic over the course of years, the indirect costs associated with travel time, gas mileage, and wear and tear on vehicles narrow the financial gap between SCIT and SLIT even more.

The cost of SLIT therapy also has a direct relationship to the total number of allergens to which the patient tests positive. The European model of SLIT solves this problem by only treating with a select few representative allergens regardless of how many allergens to which the patient tests positive. Most of the SLIT trials that come from Europe only look at the efficacy of treatment of a single antigen, the grass pollen. In Europe, only the grass pollen tablet is officially approved for use, though other SLIT preparations are quite widely available and used. Data from the European literature provides guidelines on which allergens they deem are the most critical to include in immunotherapy. In the United States, there is no comparable body of data to serve as a guideline and many practices mirror the philosophy of SCIT, using every antigen to which a patient is allergic in SLIT. Even allowing for maximum antigen usage, however, the maximum cost of SLIT in these several practices is below \$2000.

Reviewing the international literature, only 1 other study has looked at the cost of SLIT vs SCIT and has evaluated both indirect and direct medical costs. In this European study, Omnes et al.¹¹ compared the cost of SLIT with SCIT in asthmatic patients with dust mite and pollen allergies. They concluded that SLIT is economically comparable to SCIT and is an attractive option, especially in children. Another study originating from Europe concluded that SLIT is a less expensive alternative relative to SCIT when indirect costs such as loss of income and travel costs are included.¹⁰ The cost of 19 patients undergoing SLIT and 23 undergoing SCIT were compared. When both the direct and indirect costs were evaluated over a 3-year period, the expenditures per patient reached €684 vs €1004 in the SLIT and SCIT groups, respectively.

This study, to the best of our knowledge, is the only one comparing the cost of SCIT vs SLIT in the United States.

The challenges inherent in such an analysis are significant because of the widely varying insurance coverage for SCIT, as well as the arbitrary price points offered by private practices for SLIT. In general, an examination of our numbers indicate that based purely on insurance coverage, SCIT can be more cost effective for the patient than paying out-of-pocket for SLIT. However, this does not take into account indirect costs and expenses as well as time and effort saved from weekly 20-minute shot appointments, which may be required for several years. Also, insurance coverage needs to be optimal, with total or near total coverage required. We found that as soon as plans required patients to pay 20% or more of healthcare costs and/or required weekly co-pays for shot visits, the gap between SCIT and SLIT significantly narrowed. When indirect costs are then esti-

mated and factored in, the difference in cost rapidly became negligible.

Conclusion

Although the lack of insurance coverage for SLIT currently makes it more expensive than SCIT, we have found that the financial gap is much smaller than initially thought, especially when indirect costs and suboptimal coverage plans are factored in. Overall, the safety, efficacy, and convenience of SLIT may ultimately justify its increased out-of-pocket expense. Future research will focus on more national data on insurance coverage of SCIT, more information on pricing of SLIT from private allergy practices, and a more detailed breakdown of the indirect costs of weekly shot visits. 

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