

# Health Economics of Allergy Immunotherapy

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*Allergic rhinitis (AR) is a highly prevalent condition with significant morbidity, and it exacts a substantial economic burden. Direct health care expenditures attributable to AR are estimated at \$5.2 billion in 2007 dollars and indirect costs are estimated at \$6.9 billion. A growing number of studies have examined the economic benefits of allergy immunotherapy (IT), a treatment that has been shown to effectively reduce AR symptoms and alter the course of the disease. This article summarizes and critically evaluates all published economic studies of IT for the treatment of AR and asthma, with the goal of determining whether IT is economically justified as a treatment option for appropriate patients who have AR and/or asthma.*

Allergic rhinitis (AR) is a highly prevalent condition with significant morbidity, and it is responsible for substantial health care costs. An increasing number of published studies suggest that allergy immunotherapy (IT) may reduce the economic burden of AR. The purpose of this review is to critically examine these studies in detail.

## Economic Impact of Allergic Rhinitis and Asthma

Allergies are estimated to cost the US health care system in excess of \$18 billion annually, with the majority of costs attributable to asthma and a smaller proportion to AR.<sup>1</sup>

With respect to direct costs, the 1996 Medical Expenditures Panel Survey (MEPS) estimated that health care expenditures for AR were \$3.4 billion (\$5.2 billion in 2007 dollars).<sup>2</sup>

Outpatient visits (approximately 16.7 million annually<sup>2</sup>) account for just over half (52%) of AR direct costs, with prescription medications constituting the remainder (46.6%).<sup>3</sup> It is noteworthy that MEPS excluded costs of OTC medications, which are commonly used by patients with mild disease and may equal the costs attributed to prescription medications.<sup>4</sup> Asthma accounts for about 12.8 million physician office visits, 1.8 million emergency department visits, and 489,000 hospital admissions per year.<sup>5</sup> Health care use related to asthma is estimated to total \$14.7 billion annually, with prescription medications accounting for \$6.2 billion, hospital care \$4.7 billion, and physician services \$3.8 billion.<sup>5</sup> Because about 50% of asthma cases are due to allergy, direct costs of allergic asthma may be significant.

The indirect costs associated

with allergy-related mortality, absenteeism, lost productivity, and performance deficits are substantial. AR is associated with 3.8 million lost workdays per year.<sup>1</sup> Using data from the 1995 National Health Interview Survey, including workers' reports of lost productivity because of AR and use of sedating antihistamines, Crystal-Peters and associates<sup>6</sup> estimated indirect costs of AR at \$4.6 billion in 1998 (\$6.6 billion in 2007 dollars). Asthma is responsible for more than 5000 deaths, 12.8 million lost school days, and 24.5 million lost workdays each year.<sup>5</sup> In 2004, lost productivity caused by asthma-related mortality and morbidity totaled about \$4.6 billion (\$5.2 billion in 2007 dollars).<sup>5</sup>

## Economic Analyses of IT for Treatment of Allergic Rhinitis

Studies evaluating the economic benefits of IT in patients with AR and/or asthma have employed diverse methods, including 1 based on the findings of a prospective randomized trial,<sup>7</sup> 6 based on retrospective analyses,<sup>8-13</sup> and 6 based on an economic modeling approach (Table 1).<sup>14-19</sup> We critically examine each of these studies in detail. Costs reported in foreign currencies are translated into US dollars using specified exchange rates but are not updated to reflect current dollar values.

*Economic analysis based on a prospective randomized trial.* An economic analysis of subcutaneous IT (SCIT) was performed using data from a prospective single-site study in which 30 Italian adults who had pollen-induced rhinitis and asthma

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were randomly assigned to receive 3 years of SCIT plus pharmacotherapy ( $n = 20$ ) or pharmacotherapy alone ( $n = 10$ ) and monitored for 3 years after completion of SCIT.<sup>7</sup> During the pollen season, patients recorded symptom scores, allergy medication use, adverse drug reactions, and number of office visits and SCIT injections. Patients in the SCIT-plus-pharmacotherapy group began to show a significant reduction in allergy symptoms and medication use compared with the pharmacotherapy-only group in the first year of treatment; effects continued throughout the 6-year study.

The mean annual direct cost of treatment in the SCIT-plus-pharmacotherapy group was similar to that for the pharmacotherapy-only group during the first 2 years of treatment. In the third year, the SCIT-plus-pharmacotherapy group showed a 48% reduction in cost ( $P < .0001$ ) compared with the pharmacotherapy-only group. Cost reductions increased such that by year 6, annual costs were 80% lower (\$830) in the SCIT-plus-pharmacotherapy group. Maximum cost benefits occurred 3 years after discontinuation of SCIT, indicating the importance of a long-term perspective when evaluating the economic impact of IT. Disadvantages of the study included reliance on patient self-reports; failure to account for hospital admissions or emergency department visits (except in cases of adverse drug reactions); limited generalizability of the sample (adults with seasonal AR and asthma from a single allergy treatment center); and small sample size.

*Economic analyses based on retrospective claims, medical records, or survey data.* Economic analyses of IT based on retrospective claims, medical records, or survey data have been conducted in the United States,<sup>10-12</sup> France,<sup>13</sup> Italy,<sup>14</sup> and Denmark.<sup>9</sup> In a retrospective claims anal-

ysis of 603 US HMO enrollees with AR and/or asthma who received at least 1 SCIT injection and who had maintained continuous enrollment during the year before and 2 years after their first SCIT administration, investigators found that only one third of patients who started SCIT completed the desired 3.5-year course of treatment.<sup>10</sup> Beyond costs for SCIT, patients who completed at least 3.5 years of treatment had higher allergy-related costs (mostly due to higher prescription drug costs) than patients who received SCIT for less than 3.5 years (mean, \$508 vs \$421 per person-year). Higher costs for patients with longer duration of treatment may have been due to several factors. First, the costs of asthma and AR treatment for SCIT completers were 30% higher than for non-completers during the year before starting SCIT, suggesting greater disease burden. Second, follow-up after treatment (mean, 7 months) may have been too brief to begin to see a cost reduction. Third, SCIT patients who completed 3.5 years of IT may also have been more likely to demonstrate good adherence to costly medication regimens.

In another US retrospective analysis, data from a 1996 American College of Allergy, Asthma, and Immunology report<sup>20</sup> were used to compare the average cost of SCIT versus pharmacotherapy over 5 years.<sup>11</sup> Three allergy treatment centers provided the basis for estimating the 5-year costs of SCIT, which totaled about \$5000 per patient. The 5-year costs for pharmacological treatment of AR, estimated at \$10,200 per patient, were based on the assumption that persons with AR would require daily use of an antihistamine/decongestant and intranasal corticosteroid spray. This rough comparison of IT and pharmacotherapy costs has major flaws. First, estimates of the cost of pharmacological treat-

ment were based on assumed rather than actual use. Second, investigators failed to account for the cost of concomitant allergy medications used by patients receiving SCIT. Third, researchers did not consider medical costs aside from those directly associated with the administration and cost of allergy medication or SCIT. Finally, researchers failed to account for the longer-term benefits of SCIT.

Most recently in the United States, investigators conducted a 7-year (1997 to 2004) retrospective analysis of Florida Medicaid claims data to examine the economic impact of SCIT in children in whom AR was newly diagnosed.<sup>12</sup> Although only 16% of 354 patients completed at least 3 years of SCIT, pharmacy, outpatient, and inpatient costs were significantly reduced in the 6 months post-SCIT compared with the 6 months before SCIT. The main limitations of this study were its short-term follow-up, the specialized nature of the sample (Medicaid-enrolled children), and poor SCIT persistence rate.

In a French study, costs for 1000 patients who had received SCIT were estimated based on a patient survey of allergy symptoms, allergy treatments received, physician visits, allergy-related hospitalizations, and work missed in the previous 15 days.<sup>13</sup> The cost of medications for symptomatic relief was significantly lower in patients who had received SCIT for 1 to 2 years than for those who had received SCIT for less than 1 year but was not reduced in those who used SCIT longer than 2 years versus less than 1 year. The value of this study is limited by the use of patient survey data, which is vulnerable to self-selection and/or biases (149 refused to participate); estimating costs over only 15 days; and a low persistence rate.

In another study, Berto and co-

workers<sup>8</sup> analyzed the medical records of 135 children with AR and/or asthma at a single allergy center in Italy. Direct costs were based on physician office visits, pharmacological treatment, and use of sublingual allergy immunotherapy (SLIT) but excluded hospitalizations and diagnostic tests. Indirect costs were estimated using school absences, which served as a proxy for the number of lost workdays for parents. The mean cost per patient was \$481 during the year before starting SLIT and \$213 per year during the 3 years of SLIT (euro values were converted to 2002 US dollars using the exchange rate of 1 euro = \$0.95). When indirect costs were included, the total cost per patient decreased from \$2538 in the year before SLIT to \$598 per year during SLIT.

This study was limited by the lack of statistical significance testing, making it impossible to conclude that SLIT significantly reduced direct or total costs; the exclusion of some health care costs, which may have underestimated cost reductions associated with SLIT; and use of a single allergy center.

A 6-year retrospective analysis (1 year before SCIT, 4 years during SCIT, 1 year after SCIT) involving 253 adults who received SCIT at a hospital or allergy specialist office in Denmark from 1996 to 2002 is one of the few studies that failed to find a reduction in direct costs related to IT.<sup>9</sup> Patients were surveyed regarding their use of emergency departments and hospital admissions. Out-patient visit data were generally available from local county records during 1997 to 2002. Although the total mean direct cost per patient decreased from \$328 in the year before SCIT to \$169 in the year after SCIT, the average cost of 4 years of SCIT (\$3498) exceeded that for 4 years of symptomatic treatment (ST) (\$1190).

When indirect costs were in-

cluded in the analysis, there was a net savings of \$2521 during the initial 4 years of SCIT and an additional savings of \$1503 per annum in each subsequent year after SCIT completion. This study had several significant methodological flaws. Pre-SCIT medication use was based on an entirely different cohort from the study sample. The extrapolation of 7 months of post-SCIT medication use data may have overestimated post-SCIT medication use because the 7-month period included the grass pollen season when allergy medication use peaks. In addition, patients were monitored for only 1 year after SCIT was completed, which may have underestimated potential long-term reductions in costs.

*Economic modeling analyses.* A cost-utility analysis was conducted using data from an international, double-blind, placebo-controlled trial in which 316 patients were randomized to a preseasonal grass allergen tablet and 318 to placebo.<sup>16</sup> Health care utilization (physician visits, allergy medications, hospitalizations), time missed from work because of AR, and quality of life data were collected prospectively using patient diaries and surveys. For patients receiving placebo, the annual number of physician visits was estimated using data from a European survey rather than from the patient diaries. Quality-adjusted life years (QALYs), which measure the patient's health-related quality of life on a scale from 0 (death) to 1 (perfect health), were assessed during a single pollen season and were extrapolated to the end of the 9-year study period. SLIT-treated patients gained 0.0287 QALYs per season (0.222 QALYs over 9 years) compared with patients receiving placebo ( $P < .001$ ). No patients were hospitalized and there were no significant differences between groups in the number of physician visits during the pollen

season. The mean use of symptomatic medications and hours of lost work because of AR were significantly higher in the placebo group.

From a payer perspective, assuming an annual cost of SLIT of \$1860, the cost per QALY gained ranged from \$16,033 in the Netherlands to \$22,646 in Germany (2005 euro values were converted to 2005 US dollars using the exchange rate of 1 euro = \$1.24); these were below the £20,000 to £30,000 (\$40,000 to \$60,000) threshold for cost-effective therapies established by the National Institute for Clinical Excellence (NICE), United Kingdom.<sup>21</sup> Although this study incorporated data from a large, well-controlled clinical trial, the trial was relatively short in duration, and extrapolation of outcomes to 9 years may have resulted in overestimation or underestimation of cost-effectiveness.

Keiding and Jørgensen<sup>17</sup> conducted a 9-year cost-effectiveness analysis of SCIT based on results of the UK Immunotherapy Study Group (UKIS) trial, a 1-year, multicenter, randomized, double-blind study comparing SCIT with placebo in patients with pollen-induced rhinoconjunctivitis whose symptoms were uncontrolled using ST. Symptoms, medication for the symptomatic relief of allergies (available throughout the study for both groups), and quality of life were assessed before and after a 15-week pollen season.

The direct costs of treatment were estimated by combining study-related health care resource use with national price data from 6 European countries. Aside from patient-reported medication use and investigator-reported physician visits for SCIT administration, other health care resources use does not appear to have been captured. Differences between groups in the use of symptomatic medications observed during the

**Table. Summary of IT Economic Analyses**

Study, Place	Design	Sample	Results
Ariano 2006 <sup>7</sup> Italy	Prospective, randomized, open, parallel-group trial	30 adults with AR and/or asthma SCIT + drug therapy (n = 20) Drug therapy alone (n = 10)	MCD = SCIT – drug therapy MCD Year 1: \$90 (NS) MCD Year 2: –\$149 (NS) MCD Year 3: –\$504 (P < .0001) MCD Year 4: –\$821 (P < .0001) MCD Year 5: –\$825 (P < .0001) MCD Year 6: –\$830 (P < .0001)
Donahue 1999 <sup>10</sup> United States	Retrospective administrative claims analysis (HMO)	603 adults and children with AR and/or asthma 33% (n = 128) completed 3.5 years of SCIT	MCD = Completed SCIT – discontinued IT Annual cost difference (SCIT): \$698 – \$508 = \$190 Annual cost difference (non-SCIT): \$421 – \$247 = \$174
Bernstein 2004 <sup>11</sup> United States	Retrospective analysis	3 allergy treatment centers	5-year total costs of SCIT: \$4560 – \$4773 5-year total costs of drug therapy: \$10,200
Hankin 2008 <sup>12</sup> United States	Retrospective administrative claims analysis (Medicaid)	354 children with AR with or without asthma	MCD = 6 months pre-SCIT – 6 months post-SCIT Pharmacy: –\$54 Outpatient: –\$233 Inpatient: –\$2316 Total: –\$215
Le Pen 1997 <sup>13</sup> France	Retrospective analysis of patient survey data	851 allergy patients who received SCIT of varying duration	15-day cost of symptomatic medications: < 1 year SCIT: ~\$22 1 - 2 years SCIT: ~\$14
Berto 2005 <sup>8</sup> Italy	Retrospective administrative claims analysis	135 children and adolescents with AR and/or asthma receiving 3 years of SLIT	MCD = Year before SLIT – year after SLIT MCD (direct): \$481 vs \$213 MCD (indirect): \$2538 vs \$598
Pedersen 2005 <sup>9</sup> Denmark	Retrospective administrative claims analysis	253 adults with AR and/or asthma who received SCIT during 1996 - 2002	Mean direct cost per patient (pre-SCIT): \$328; mean direct cost per patient (post-SCIT): \$169 Mean direct cost per patient (4 years SCIT): \$3498 Mean cost per patient (4 years ST): \$1190

IT, allergy immunotherapy; AR, allergic rhinitis; SCIT, subcutaneous allergy immunotherapy; MCD, mean cost difference per patient; NS, non-significant; SLIT, sublingual allergy immunotherapy; ST, symptomatic treatment; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Study, Place	Design	Sample	Results
Bachert 2007 <sup>16</sup> 7 European countries	Economic modeling study	634 adults with rhinoconjunctivitis SCIT (n = 316) Placebo (n = 318)	Payer perspective (annual cost of SCIT \$1860): cost per QALY ranged from \$16,033 in the Netherlands to \$22,646 in Germany
Keiding 2007 <sup>17</sup> 6 European countries	Economic modeling study	410 adults with seasonal rhinoconjunctivitis uncontrolled by ST SCIT (n = 307) Placebo (n = 103)	Payer perspective: the ICER for SCIT vs ST per symptom-free day and well day ranged from \$32 (Austria) to \$84 (Netherlands) and from \$30 (Austria) to \$76 (Netherlands), respectively. Societal perspective: SCIT dominated ST in 4 of the 6 countries for both variables. Payer perspective: cost per QALY ranged from \$12,048 to \$32,070. Societal perspective: SCIT was dominant over ST in all countries except the Netherlands and Sweden.
Omnes 2007 <sup>19</sup> France	Economic modeling study	1000 hypothetical adult and child patients with AR who received SCIT or SLIT (3 or 4 years), or ST over 7 or 8 years	ICER per additional improved patient for SCIT vs ST ranged from \$253 to \$816 and for SLIT vs ST ranged from \$712 to \$2679 ICER per additional case asthma avoided for SCIT vs ST ranged from \$444 to \$1500 and for SLIT vs ST ranged from \$931 to \$4450
Berto 2006 <sup>14</sup> Italy	Economic modeling study	1000 hypothetical adults with AR receiving SLIT for 3 years and monitored for 6 years vs SC for 6 years	SLIT was dominant over ST from a payer and societal perspective. 6-year mean savings per patient SLIT vs ST: \$908 (payer perspective), \$2662 (societal perspective).
Schadlich 2000 <sup>15</sup> Germany	Economic modeling study	1000 hypothetical adults with AR receiving SCIT for 3 years vs ST and monitored for 10 years	Break-even point reached between year 6 and 8. Net savings of \$377 (payer) to \$690 (societal) per patient over 10 years 10-year ICER (payer) per additional asthma case avoided for SCIT vs ST: -\$2111 to -\$2361
Buchner 1995 <sup>18</sup> Germany	Economic modeling study	Estimated mean 10-year per-patient total cost of AR and asthma patients receiving ST vs SCIT	Break-even point reached after 6 years of treatment in AR and 4 years of treatment in asthma patients MCD = 10 years ST – 10 years SCIT MCD per AR patient: \$6853 – \$3771 = \$3082 MCD per asthma patient: \$10,187 – \$4246 = \$5941

clinical trial were assumed to continue through the remaining 8 years. Indirect costs were estimated using the number of workdays lost in a previous study of rhinoconjunctivitis. Treatment effects were measured as the percentage of symptom-free days (31.2% for SCIT and 23.6% for ST) and well days (36.6% for SCIT and 28.2% for ST) during the pollen season.

The incremental cost-effectiveness ratio (ICER), calculated as the cost difference between SCIT and ST divided by the difference in effect, for direct cost per symptom-free day and well day ranged from \$32 in Austria to \$84 in the Netherlands and from \$30 in Austria to \$76 in the Netherlands, respectively (2005 euro values were converted to 2005 US dollars using the exchange rate of 1 euro = \$1.24). When indirect costs were included, SCIT demonstrated reduced costs and increased effects in 4 of the 6 countries per symptom-free and well days. When only direct costs were considered, the cost-effectiveness ratio ranged from \$12,048 to \$32,070 per QALY, all below the NICE threshold for cost-effective therapies.<sup>21</sup> When indirect costs were included, the cost-effectiveness ratio was higher for SCIT than for ST in all countries except the Netherlands (\$8008 per QALY) and Sweden (\$6230 per QALY). Sensitivity analyses showed that only very considerable changes in the base values of key variables caused the cost-effectiveness ratios to exceed \$60,000.

As with the previous study, investigators extrapolated short-term costs and effects to 9 years, which may have underestimated the cost savings associated with SCIT by failing to account for the potential reduction in the use of health care resources over time (because of lower rates of asthma and other comorbid disorders) among those receiving SCIT. Further, results may have been

affected by the failure to assess non-allergy-related outpatient visits, inpatient care, and emergency department use.

A third cost-effectiveness analysis conducted from a French health plan perspective compared SCIT, SLIT, and ST in patients with AR and/or asthma caused by pollen or dust mite allergies.<sup>19</sup> This study used a Delphi expert panel to populate a decision tree model with both efficacy (number of improved patients and asthma cases avoided) and resource use variables (clinic visits, diagnosis and follow-up tests, drugs, and IT); hospitalizations were not included. The model time horizon was 6 years for adults and 7 for children, and patients were assumed to have received IT for 3 (adults) or 4 (children) years. IT was found to be more effective than ST, but ST was the least costly treatment. SCIT was more cost-effective than SLIT. The ICER per additional improved patient for SCIT versus ST ranged from \$253 to \$816, and the ICER per additional case of asthma avoided ranged from \$444 to \$1500 (2003 euro values were converted to US dollars using the exchange rate of 1 euro = \$1.13). The ICER per additional improved patient for SLIT with ST ranged from \$712 to \$2679, and the ICER per additional case of asthma avoided ranged from \$931 to \$4450.

The main limitation of this study was its use of an expert panel to estimate both efficacy and health care resource variables. Although decision models commonly use expert opinions to develop and populate models, groups of experts often disagree and the notion of expert "consensus" may be an illusion.<sup>22</sup> The authors claimed to have "cross-validated" the medical outcomes of the model with those of published clinical trials, but it is not clear whether these clinical trials were selected to develop the model efficacy parameters

(and whether other trial data were rejected) or whether these parameters were estimated using other sources. In addition, although the expert panel excluded inpatient costs from the model based on the assumption that hospitalization was a rare event, subsequent examination of French retrospective data indicated that hospitalization of asthmatic children and adults was frequent enough to have been included in the model and that failure to include these costs probably underestimated the cost-effectiveness of IT compared with ST.

The Sublingual Immunotherapy Pollen Allergy Italy (SPAI) study compared costs, clinical outcomes, and cost-effectiveness ratios for SLIT with pharmacotherapy versus pharmacotherapy alone.<sup>14</sup> A decision tree model was populated using retrospective data from the clinical records of 100 young adults (aged 16 to 45 years) with pollen-induced AR with or without asthma. Retrospective data included allergy treatments, health care resources, physician ratings of improvement, and patient diagnoses; however, the sources of various health care resource data were unclear. Direct costs included physician office visits, diagnostic procedures, hospitalizations, SLIT, and anti-allergy drugs; indirect costs included lost workdays. The costs of SLIT and anti-allergy medications were based on recommended dosing schedules rather than actual use. A physician panel estimated the number of follow-up visits per year by disease severity; similar rates of hospitalizations were applied to both treatment groups.

The 6-year mean direct cost per patient was \$2395 for 3 years of SLIT plus pharmacotherapy (including 3 years of follow-up after SLIT discontinuation) versus \$3026 for 6 years of pharmacotherapy alone (the study authors converted euros to US

dollars using the exchange rate of 1 euro = \$1.26). From the payer perspective, the cost per additional improved patient was \$5434 for SLIT plus pharmacotherapy and \$8097 for pharmacotherapy alone; cost per additional asthma case avoided was \$2396 for SLIT plus pharmacotherapy and \$3304 for pharmacotherapy alone. Several methodological issues should be noted. First, although health care utilization data were supposedly derived from patient clinical records, investigators failed to specify the precise methods used to estimate these outcomes. Second, use of allergy medications and SLIT were not based on actual use. Third, the end points for the cost-effective analysis—patient improvement and asthma prevention—were derived from unblinded physician ratings of their own patients.

Another study used multiple sources to model health outcomes associated with 3 years of SCIT versus ST in persons with AR during 10 years of follow-up.<sup>15</sup> The total direct costs associated with SCIT were higher for the first 6 years, after which SCIT became cost-saving relative to pharmacotherapy. The average net savings (1997 dollars) per patient over 10 years ranged from \$377 (SCIT for pollen allergy from payer perspective) to \$690 (SCIT for pollen allergy from societal perspective) (the study authors converted deutsche marks (DM) to US dollars using the exchange rate of 1 DM = \$0.58).

A decision tree model was then constructed using clinical trial data. From the payer perspective, the ICER per additional patient free from asthma symptoms for SCIT versus ST ranged from \$2111 (mite allergy) to \$2361 (pollen allergy) during a 10-year period. SCIT was dominant from the perspective of society, the health care system, and payers in Germany. Although this study used a sophisticated model, estimation of

cost savings was based strictly on the potential of SCIT to reduce the risk of developing asthma. In addition, the model assumed that patients were 100% adherent to SCIT; this assumption contradicts SCIT adherence data reported elsewhere.<sup>10,23-26</sup>

A study by German researchers described a theoretical cost-benefit analysis of SCIT for the treatment of AR and allergic asthma.<sup>18</sup> The model assumptions included a 90% therapeutic success rate for SCIT (based on a systematic literature review), a 10-year duration of efficacy, and further assumed that 43% of patients receiving ST or unsuccessful SCIT would develop asthma after 8 years. Results of the analysis indicated that the cost advantage for ST shifted to SCIT during the sixth year of treatment for AR. After 10 years, the total cost per AR patient treated with standard therapy was \$6853 compared with \$3771 for SCIT (1990 DM values were converted to 1990 US dollars using the exchange rate of 1 DM = \$0.62). The cost advantage shifted to SCIT during the fourth year of treatment for allergic asthma. After 10 years, the total cost per asthma patient treated with ST was \$10,187 compared with \$4246 for SCIT. This relatively simplistic model had several limitations. No sensitivity analyses were conducted to test the robustness of the model. In addition, the model examined patients with AR and asthma separately and did not account for co-occurring disorders at treatment initiation.

## Conclusion

A growing and diverse body of literature supports the economic benefits of IT. There are unique limitations associated with each type of economic analysis included in this review. Although prospective randomized trials offer the greatest potential for controlling variables, clinical trials may be limited by bias

introduced because of the increased attention and monitoring patients receive, use of short time horizons, and recruitment of unrepresentative patients.<sup>27</sup> In comparison, administrative claims data do not allow for control of variables but offer objective information about medical resource use by patients receiving allergy treatment in a real-world setting. Because of poor treatment persistence, however, administrative claims data may underestimate potential cost benefits, and such data are limited with respect to measuring the clinical benefits of IT. Although economic modeling studies have consistently found IT to yield cost advantages relative to standard drug treatment over an 8- to 10-year period,<sup>14-19</sup> the assumptions underlying these analyses have not been adequately validated.

Despite the use of widely varying study designs, patient samples, and methodologies, the economic analyses of IT conducted to date have consistently shown that IT reduces direct and indirect costs. The magnitude of cost savings associated with IT varied across studies, with up to an 80% reduction in costs seen 3 years after completion of IT.<sup>7</sup> Given that cost savings are likely to peak once IT has been completed, demonstration of the long-term cost savings associated with IT is an important goal for future research. Because longitudinal studies conducted to date in the United States have found poor IT continuation rates,<sup>10,12</sup> estimated cost savings derived from these studies are likely to be conservative and may be higher for persons who complete a longer duration of treatment. ■

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