

Work smarter: click now for your **free trial**

Personal Selections for iPad



ELSEVIER

Work smarter: click now for your **free trial**

Personal Selections for iPad



ELSEVIER

Work smarter: click now for your **free trial**

Personal Selections for iPad



ELSEVIER

ANNALS OF
Allergy, Asthma
& Immunology[Articles & Issues](#) [Quiz Image Archive](#) [For Authors](#)Search for in All Fields[« Back](#)Annals of Allergy, Asthma & Immunology
Volume 104, Issue 1, Pages 79-85, January 2010[Print or Share This Page](#)Access this article on
[SciVerse ScienceDirect](#)Allergen immunotherapy and health care cost benefits for
children with allergic rhinitis: a large-scale, retrospective,
matched cohort studyCheryl S. Hankin, PhD , Linda Cox, MD, David Lang, MD, Amy Bronstone, PhD, Paul Fass, MD, Bryan Leatherman, MD, Zhaohui Wang, MS

Received 16 July 2009; received in revised form 18 August 2009; accepted 31 August 2009.

[Abstract](#) [Full Text](#) [PDF](#) [Images](#) [References](#)

Article Outline

- I. [Abstract](#)
- II. [Introduction](#)
- III. [Methods](#)
 - A. [Florida Medicaid Data Set](#)
 - B. [Definition of Terms](#)
 - C. [Study Sample](#)
 - D. [Data Analyses](#)
- IV. [Results](#)
 - A. [Sample Identification and Characteristics](#)
 - B. [Immunotherapy Utilization](#)
 - C. [Health Care Utilization and Costs](#)
- V. [Discussion](#)
- VI. [References](#)
- VII. [Copyright](#)

Background

Children with allergic rhinitis (AR) often experience significant impairment in quality of life and health, which increases health care utilization.

Objective

To determine whether allergen immunotherapy reduces health care utilization and costs in children newly diagnosed as having AR using a retrospective matched cohort design.









Methods

Among children (age <18 years) with a Florida Medicaid paid claim between 1997 and 2007, immunotherapy-treated patients were selected who had newly diagnosed AR, who had not received immunotherapy before their first (index) AR diagnosis, who had received at least 2 immunotherapy administrations after their index AR diagnosis, and who had at least 18 months of data after their first immunotherapy administration. A control group of patients with newly diagnosed AR who had not received immunotherapy either before or subsequent to their index AR diagnosis also were identified, and up to 5 were matched with each immunotherapy-treated patient by age at first AR diagnosis, sex, race/ethnicity, and diagnosis of asthma, conjunctivitis, or atopic dermatitis.

Results

Immunotherapy-treated patients had significantly lower 18-month median per-patient total health care costs (\$3,247 vs \$4,872), outpatient costs exclusive of immunotherapy-related care (\$1,107 vs \$2,626), and pharmacy costs (\$1,108 vs \$1,316) compared with matched controls ($P < .001$ for all). The significant difference in total health care costs was evident 3 months after initiating immunotherapy and increased through study end.

Article Tools

-  [Download Images*](#)
-  [Email Abstract](#)
-  [Add to My Reading List](#)
-  [Rights/Permissions](#)
-  [Request Reprints](#)
-  [Related Articles](#)
-  [\(20\) Cited in Scopus](#)
-  [Export Citation](#)
-  [Create Citation Alert](#)
- [VIEW GENETIC INFO](#)
- * [Image Usage & Resolution](#)

Conclusions

This study demonstrates the potential for early and significant cost savings in children with AR treated with immunotherapy. Greater use of this treatment in children could significantly reduce AR-related morbidity and its economic burden.

[Back to Article Outline](#)

Introduction

Allergic rhinitis (AR) is the third most common chronic disease in children (age <18 years) in the United States,¹ with up to 40% affected.² Untreated or inadequately treated AR can substantially impair children's quality of life³ and school performance or learning ability^{4, 5, 6}; can cause sleep disturbance and daytime fatigue and somnolence⁷ and depressed mood, irritability, and behavioral problems³; and can interfere with social interaction and participation in sports and other outdoor activities.³ Untreated AR, especially in children, is associated with decreased appetite, poor growth, and failure to thrive⁴; worsening AR symptoms⁸; and a substantially increased risk of asthma, conjunctivitis, eczema, eustachian tube dysfunction, otitis media, lymphoid hypertrophy or obstructive sleep apnea, pharyngitis, and sinusitis.⁴

Each year in the United States, AR accounts for 16.7 million physician office visits (children and adults),⁹ 2 million missed school days,¹⁰ and \$2.3 million (1996 US\$) in direct costs for children younger than 12 years.¹¹ The presence of AR in children with asthma significantly increases health services use,^{12, 13} including a 250% increase in hospitalizations.¹³ Because of the serious clinical and economic consequences of AR, early diagnosis and aggressive treatment should be priorities.

Although used infrequently compared with pharmacologic treatments, allergen immunotherapy has proved to be a highly effective and safe treatment for AR.¹⁴ In contrast to pharmacologic therapies, which temporarily relieve allergy symptoms during use but do not remain effective after discontinuation,¹⁵ studies^{16, 17, 18} of immunotherapy have shown 3 to 4 years of consistent treatment results in sustained reduction of symptoms for 3 to 6 years after termination of immunotherapy. In another study, children who had received 3 years of preseasonal grass pollen immunotherapy and who experienced a significant reduction in AR symptoms relative to controls (who received pharmacotherapy) at study end continued to demonstrate significantly reduced allergy symptoms compared with the control group when evaluated at 6 years¹⁹ and 12 years²⁰ of follow-up. In addition to its long-term sustained efficacy, immunotherapy is the only treatment proved to alter the course of allergic disease as demonstrated by its association with significant reductions in the likelihood that children with AR will develop asthma^{21, 22, 23} and new sensitizations to aeroallergens.^{20, 24, 25}

Given these important benefits, immunotherapy is likely to be a cost-effective option for the management of AR. A growing number of studies have examined the cost-effectiveness of immunotherapy, but most have been conducted in Europe and have focused on adult populations.²⁶ Only 2 studies to date have examined the economic benefits of immunotherapy in adults, children, or both in the United States. In 1999, a retrospective analysis of 603 adults and children enrolled in managed care (1988–1992) with AR with or without asthma were followed up for 2 to 6 years after initiation of immunotherapy.²⁷ The per-person per-year cost of immunotherapy and nonimmunotherapy care was \$1,206 for patients who completed a full course of immunotherapy (≥3.5 years) vs \$668 for patients who discontinued immunotherapy before completing a full course. Although the results seemed to suggest that immunotherapy is more costly than other AR treatments, the authors acknowledged several caveats: (1) immunotherapy completers had higher health care costs than did noncompleters before initiating immunotherapy, possibly due to being more severely ill or more compliant with taking allergy medications, and (2) the short follow-up period (mean, 7 months) may not have allowed for accrual of significant cost savings.²⁷ More recently, Hankin and colleagues²⁸ conducted a retrospective claims analysis of 354 Florida Medicaid-enrolled children with newly diagnosed AR to determine the short-term cost savings associated with immunotherapy. The investigators found significant reductions in the use of outpatient ($P < .001$), pharmacy ($P < .001$), and inpatient ($P = .02$) services in the 6 months after vs preceding termination of immunotherapy. This reduction in health care utilization resulted in a 6-month total cost savings of \$401, which offset the average total cost of immunotherapy (\$424 per patient). Limitations of this study included the short follow-up period (6 months) and the lack of a control group.

To help resolve the conflicting results of these studies, we designed a more robust study that included a retrospective matched cohort design and a longer follow-up period (18 months). Drawing from the same Florida Medicaid database as was previously used (with 2 additional years of data),²⁸ we sought to determine whether children with newly diagnosed AR who received immunotherapy (the immunotherapy-treated group) incurred less health care utilization and fewer costs during an 18-month follow-up period compared with a matched group of AR-diagnosed children who did not receive immunotherapy (the control group).

[Back to Article Outline](#)

Methods

Florida Medicaid Data Set

Florida Medicaid provides access to health care for more than 2 million low-income individuals, and more than half of the enrollees are younger than 21 years. Computerized Florida Medicaid claims records contain basic demographic information, *International Statistical Classification of Diseases and Related Health Problems (ICD-9)* codes that indicate diagnoses, *Current Procedural Terminology* codes that indicate procedures, and National Drug Codes that indicate type and strength of medications, number of administrations per medication fill, number of days supplied per medication fill, and payment data. Information is patient de-identified and is fully compliant with the Health Insurance Portability and Accountability Act Privacy Rule. Because this observational study involved the analysis of claims data that were patient de-identified, it was exempt from review by an institutional review board.

Definition of Terms

The presence of an AR diagnosis was identified by ICD-9 code 477.X. Immunotherapy use was identified by *Current Procedural Terminology* codes 95115, 95117, 95120, 95125, 95144, 95165, 95180, and 95199. The presence of comorbid allergy-related illness was identified by the following ICD-9 codes: asthma, 493.X; atopic dermatitis, 691.8; and conjunctivitis, 372.X. Patients with newly diagnosed AR were defined as those whose first AR diagnosis was preceded by a full year in which no AR diagnoses occurred. Patients were characterized as receiving de novo immunotherapy if their first documented immunotherapy claim followed (rather than preceded) their first AR diagnosis.

Study Sample

Participants were selected from Florida Medicaid enrollees who had a paid claim between July 1, 1997, and June 30, 2007. To identify the pool of eligible immunotherapy-treated patients, first we selected patients younger than 18 years with a diagnosis of AR. Second, we retained only patients who were newly diagnosed with AR. Third, we retained those who had received de novo immunotherapy. Fourth, we excluded patients who had received fewer than 2 immunotherapy administrations after their first AR diagnosis. Finally, only those who had at least 18 months of follow-up data after initiating immunotherapy were retained.

To identify the pool of eligible control patients, we followed the first 2 steps described in the previous paragraph for selecting immunotherapy-treated patients. Then, we selected those who had not received immunotherapy preceding their first AR diagnosis. Finally, we retained only those who had no immunotherapy administrations at any time during the study.

After identifying the pools of eligible immunotherapy-treated and control patients, 1 or more control patients were matched with each immunotherapy-treated patient on the following variables: (1) age at first AR diagnosis, (2) sex, (3) race/ethnicity, and (4) diagnosis of asthma, conjunctivitis, or atopic dermatitis. Only matched control patients with at least 18 months of follow-up data after their match date were retained. Each immunotherapy-treated patient was matched with up to 5 control patients. Eligible immunotherapy-treated patients who could not be matched were excluded from further analysis.

Data Analyses

Data sets from July 1, 1997, through June 30, 2007, were provided by the Florida Medicaid Program in 30 files in compressed text format. These were decompressed and imported for analysis using statistical software (SAS/STAT version 7; SAS Institute Inc, Cary, North Carolina). As is commonly seen when analyzing data on health care utilization and cost,²⁹ data were not normally distributed but instead were highly skewed to the right (ie, a few patients had extremely high resource use and costs); we, therefore, performed Wilcoxon signed rank tests to compare the groups' 18-month median per-patient health care use and costs. Arithmetic means for health care utilization and costs are valuable in health care policy decision making and so also are presented. Health care components included total inpatient stays, total outpatient visits (with outpatient visits inclusive and exclusive of immunotherapy-related care reported separately), total pharmacy fills, and total health care use.

[Back to Article Outline](#)

Results

Sample Identification and Characteristics

The results of sample identification procedures used to determine the pool of eligible immunotherapy-treated patients and controls are shown in [Figure 1](#). There were 2,985 eligible immunotherapy-treated patients and 176,202 eligible controls. After matching, 2,771 patients in the immunotherapy-treated group and 11,010 in the matched control group remained. Among all children enrolled in Florida Medicaid between 1997 and 2007, 7.6% (264,147 of 3,472,786) received a diagnosis of AR. Among patients with newly diagnosed AR, 2.5% (4,571 of 181,682) received de novo immunotherapy.

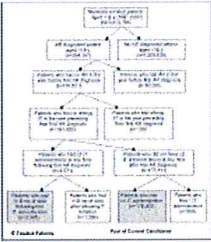


Figure 1. Flowchart of the steps used to identify the sample of patients newly diagnosed as having allergic rhinitis (AR) who received de novo immunotherapy (IT) (IT-treated patients) and the sample of patients newly diagnosed as having AR who did not receive de novo IT (potential pool of controls). Subsequently, each IT-treated patient was matched with up to 5 controls.

[View Large Image](#) | [Download to PowerPoint](#)

Immunotherapy Utilization

[Table 1](#) displays descriptive information about the use of immunotherapy in the immunotherapy-treated group (N = 2,771) during the 18 months after treatment initiation. The mean number of immunotherapy administrations received was 24, with a mean gap between immunotherapy administrations of approximately 2 weeks during induction and 3 weeks during maintenance. During induction, approximately 21% of the patients received immunotherapy injections at least every week, on average. The mean and median costs of immunotherapy during the 18-month period were \$628 and \$463, respectively.

Table 1. IT Use Across 18 Months in 2,771 IT-Treated Patients in the Matched Sample

Characteristic	Mean	SD	Median	Minimum	Maximum
IT administrations, No.	24	20	18	1	130
Time between IT administrations, da					
Induction	15.2	16.7	10.3	1	178
Maintenance	18.9	18.6	14	1	235
Total per-patient cost of IT for 18 mo, \$	628	566	463	8	3,537
Cost per IT administration, \$	31	23.6	25	5	280 ^b

Abbreviation: IT, immunotherapy.

^aInduction refers to the first 6 months of IT and maintenance refers to IT received after the first 6 months.

^bCosts at the higher end include codes for rapid desensitization, in which multiple injections are given during an accelerated induction regimen.

Health Care Utilization and Costs

Table 2 displays the 18-month median per-patient health care use and costs for the immunotherapy-treated group and matched controls who did not receive immunotherapy. Immunotherapy-treated patients had significantly lower 18-month median per-patient total health care costs (inclusive of immunotherapy costs) compared with matched controls who did not receive immunotherapy (\$3,247 vs \$4,872; $P < .001$). This cost difference was largely attributable to significantly lower 18-month median per-patient outpatient costs exclusive of immunotherapy-related care (\$1,107 vs \$2,626, $P < .001$). Immunotherapy-treated patients had significantly lower 18-month median per-patient pharmacy costs than matched controls (\$1,108 vs \$1,316; $P < .001$), but there was no significant difference in the median number of pharmacy fills. There was a trend toward lower 18-month median per-patient inpatient costs in the immunotherapy-treated group vs the matched control group (\$3,901 vs \$4,414; $P = .06$). Both groups had a similar median number of hospital stays (1.0; $P = .28$). **Table 3** provides the median per-patient health care costs for both groups at 3, 6, 12, and 18 months. Total health care costs, outpatient costs (exclusive and inclusive of immunotherapy-related care), and pharmacy costs for the immunotherapy-treated group were significantly lower than those for the matched control group as early as 3 months after initiating immunotherapy, and there continued to be significant separation between the groups at 6, 12, and 18 months. At no time did the groups significantly differ regarding inpatient costs.

Table 2. Comparison of 18-Month Median Per-Patient Health Care Utilization and Costs Between IT-Treated Patients and Matched Controls Who Received No IT

	Participants, No.		Mean value		Median value		P value ^a
	IT-treated patients	Matched controls	IT-treated patients	Matched controls	IT-treated patients	Matched controls	
Health Care Claims							
Inpatient stays, No.	75	98	1.5	3.1	1.0	1.0	.28
Outpatient visits, total No.	2,767	10,757	46.0	51.8	36.0	30.0	.29
Outpatient ^b	2,711	10,529	24.5	47.4	15.0	30.4	<.001
IT	2,771	NA	24.1	NA	18.0	NA	
Pharmacy fills, total No.	2,668	10,029	28.7	28.4	22.0	23.2	.15
Health Care Costs							
Total inpatient costs, \$	75	98	6,679	13,479	3,901	4,414	.06
Total outpatient costs, \$	2,767	10,757	3,268	7,664	1,829	2,594	<.001
Outpatient ^b	2,711	10,529	2,388	6,618	1,107	2,626	<.001
IT	2,771	NA	628	NA	463	NA	
Total pharmacy costs, \$	2,668	10,029	1,838	2,781	1,108	1,316	<.001
Total health care costs, \$ ^c	2,769	10,834	5,006	11,733	3,247	4,872	<.001

Abbreviations: IT, immunotherapy; NA, not applicable.

^aP values are for Wilcoxon signed rank tests comparing medians of the IT treatment and matched control groups.

^bExcludes outpatient visits related to IT or the cost of IT.

^cIncludes the cost of IT.

Table 3. Differences in Health Care Costs^a Between IT-Treated Patients and Matched Controls During 18-Month Follow-up

Cost category	Study time points				Between-group differences
	3 mo	6 mo	12 mo	18 mo	
Total health care costs, \$					
IT-treated patients	790	1,347	2,345	3,247	$P < .001$ at all time points
Matched controls	1,038	1,874	3,406	4,872	

Inpatient costs, \$					
IT-treated patients	1,770	3,057	2,918	3,901	Nonsignificant at all time points
Matched controls	2,573	2,754	4,682	4,414	
Outpatient costs exclusive of IT, \$					
IT-treated patients	239	416	772	1,107	$P < .001$ at all time points
Matched controls	644	1,107	1,903	2,626	
Outpatient costs inclusive of IT, \$					
IT-treated patients	465	805	1,358	1,829	$P < .001$ at all time points
Matched controls	635	1,086	1,887	2,594	
Pharmacy costs, \$					
IT treated patients	272	465	829	1,108	$P < .001$ at all time points
Matched controls	316	533	936	1,316	

Abbreviation: IT, immunotherapy.

^aAll costs are median and per patient.

[Back to Article Outline](#)

Discussion

In this retrospective, matched cohort study, we compared matched groups of children with newly diagnosed AR who either did or did not receive immunotherapy after their first AR diagnosis. Even after matching groups by sex, race/ethnicity, age at first AR diagnosis, and the presence of AR-related comorbid illnesses (asthma, conjunctivitis, and atopic dermatitis), patients in the immunotherapy-treated group incurred 33% (\$1,625) lower 18-month median per-patient overall health care costs; 29% (\$765) to 58% (\$1,519) lower outpatient costs; and 16% (\$208) lower pharmacy costs ($P < .001$ for all) after immunotherapy initiation. Furthermore, these significant reductions were evident as early as 3 months after immunotherapy initiation and increased during the 18-month follow-up period.

These findings confirm and strengthen those of earlier studies. In a previous study,²⁸ we found that the cost of immunotherapy was offset by the cost savings accrued during the 6 months after immunotherapy completion, but we did not find additional cost savings. An Italian retrospective study³⁰ compared the average direct health care costs of 135 children and adolescents with AR and asthma, asthma alone, or AR, asthma, and conjunctivitis during the year before immunotherapy was initiated with those accrued during the 3 years of immunotherapy. Compared with the year before immunotherapy initiation, the average annual per-patient total health care cost was 56% lower during the 3 years of immunotherapy. The investigators also found no significant difference in the average annual per-patient direct health care costs (>4 years) for a subset of asthmatic patients who had received immunotherapy ($n = 41$) and a matched sample of asthmatic patients who did not receive immunotherapy. Ariano et al³¹ conducted a 6-year prospective study in which 30 patients with seasonal rhinitis and asthma were randomly assigned to receive 3 years of immunotherapy or pharmacologic treatment and then were followed up for an additional 3 years after completing treatment. Although no significant cost differences were seen in the first year of treatment, immunotherapy-treated patients had 15% ($P < .001$) and 48% ($P < .001$) lower health care costs in the second and third years of treatment, respectively. These statistically significant cost differences were maintained during the 3 years after immunotherapy discontinuation and peaked at 80% ($P < .001$) in the sixth year of the study (third year after immunotherapy termination). The average annual net savings after more than 6 years was \$830. In addition to these retrospective and prospective cost studies, several European economic modeling studies have provided support for the cost-effectiveness of immunotherapy.²⁶

Several limitations should be mentioned about the present study. First, we sought to match patients on potentially confounding variables but may have overlooked or been unable to control for other important characteristics, such as patient adherence to pharmacologic medications and use of allergen avoidance interventions. Allergen avoidance interventions are recommended as a first step in allergy treatment, but there are no procedural codes associated with educating families about these methods, and so we could not determine whether immunotherapy-treated patients and matched controls were equally likely to receive information about allergen avoidance, and neither did we have information regarding parents' implementation of recommended avoidance measures. Second, because this was a retrospective, observational study, we cannot make assumptions about causality. Third, because study participants were enrolled in a public health care plan, findings may not generalize to individuals receiving care through private health care systems. Finally, although several studies, including the present study, have found that immunotherapy-related cost savings increase across time,³¹ the duration of follow-up (18 months) was limited by the relatively few participants who had received immunotherapy and who were continuously enrolled throughout the study (≥ 12 months before and 18 months after immunotherapy initiation).

Children with AR may be even more vulnerable than adults to undertreatment because they may be unable to verbalize their symptoms,³² frequently do not complain of symptoms specific to AR,^{4, 8} and often present with recurrent sore throats or upper respiratory tract infections.⁴ Consequently, physicians may misattribute these symptoms to colds or viral infections,³³ resulting in multiple unnecessary courses of antibiotics.⁴

Immunotherapy remains an underused treatment for AR in the United States and elsewhere despite the large body of evidence that supports its effectiveness and safety for the treatment of AR,³⁴ including its unique properties as an allergic disease-modifying treatment.^{20, 21, 22, 23, 24, 25, 35} Studies^{27, 28, 36} have shown that only 3% to 5% of US children and adults with AR, asthma, or both have received immunotherapy. In a randomly selected representative sample of 726 adolescents and adults (age range, 14–44 years) in Denmark screened for the presence of respiratory symptoms and treatment, and subsequently physician diagnosed as having AR, asthma, or both, only 2% ($n = 12$) reported currently receiving immunotherapy.³⁷ Investigators' careful evaluation of each participant revealed that 12 persons with allergic asthma with or

without AR (2%; 12 of 493), 219 persons with moderate-to-severe AR with or without asthma (31%), and 146 with AR and asthma (21%) were clinically appropriate for immunotherapy. Thus, although only 12 persons were currently receiving immunotherapy, 377 should have been considered for the treatment of AR or asthma with immunotherapy.

The data reported in this study and in others noted previously herein suggest that we are missing an opportunity to significantly improve health outcomes and reduce health care costs by underusing immunotherapy when appropriate. Possible reasons for the underuse of immunotherapy include lack of primary care physician training in identifying patients appropriate for referral and specialty immunotherapy evaluation³⁸ and concerns about the safety and appropriateness of immunotherapy, especially in young children.³⁹ Studies^{40, 41, 42} have reported poor patient compliance with immunotherapy, and improved adherence is likely to increase treatment effectiveness, improve patient health, and further reduce health care costs. However, poor adherence is an insufficient explanation for the particularly low use of immunotherapy given that allergy medications, the most commonly prescribed treatment for AR, are also associated with low adherence rates.⁴³

In summary, this is the second US-based study to demonstrate substantial health care cost savings associated with immunotherapy and provides even stronger evidence for the cost benefits of this allergy treatment than our previous study.²⁸ Furthermore, this is the first study to show a significant separation between immunotherapy-treated patients and matched control patients in health care costs as early as 3 months after treatment initiation. The present data suggest that more frequent use of immunotherapy in the United States could lead not only to improved clinical outcomes but also to early and consistent reduced direct medical expenditures in children with AR.

[Back to Article Outline](#)

References

1. National Academy on an Aging Society. **Chronic Conditions: A Challenge for the 21st Century**. Washington, DC: National Academy on an Aging Society; November 1999;
[View In Article](#)
2. Wright AL, Holberg CG, Martinez FD. **Epidemiology of physician-diagnosed allergic rhinitis in childhood**. *Pediatrics*. 1994;94:895-901
[View In Article](#) | [MEDLINE](#)
3. Meltzer EO. **Quality of life in adults and children with allergic rhinitis**. *J Allergy Clin Immunol*. 2001;108:S45-S53
[View In Article](#) | [Abstract](#) | [Full-Text PDF \(193 KB\)](#) | [CrossRef](#)
4. Lack G. **Pediatric allergic rhinitis and comorbid disorders**. *J Allergy Clin Immunol*. 2001;108(suppl):S9-S15
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(94 KB\)](#) | [CrossRef](#)
5. Sundberg R, Toren K, Hoglund D, Aberg N, Brisman J. **Nasal symptoms are associated with school performance in adolescents**. *J Adolesc Health*. 2007;40:581-583
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(67 KB\)](#) | [CrossRef](#)
6. Walker S, Khan-Wasti S, Fletcher M, Cullinan P, Harris J, Sheikh A. **Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study**. *J Allergy Clin Immunol*. 2007;120:381-387
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(129 KB\)](#) | [CrossRef](#)
7. Leger D, Annesi-Maesano I, Carat F, et al. **Allergic rhinitis and its consequences on quality of sleep: an unexplored area**. *Arch Intern Med*. 2006;166:1744-1748
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
8. Stewart MG. **Identification and management of undiagnosed and undertreated allergic rhinitis in adults and children**. *Clin Exp Allergy*. 2008;38:751-760
[View In Article](#) | [CrossRef](#)
9. Cherry DK, Burt CW, Woodwell DA. **National Ambulatory Medical Survey: 1999 summary**. *Adv Data Vital Health Stat*. 2001;322:1-36
[View In Article](#)
10. American Academy of Allergy Asthma and Immunology Task Force on Allergic Disorders. **Promoting Best Practice: Raising the Standard of Care for Patients With Allergic Disorders: Executive Summary Report**. Milwaukee, WI: American Academy of Allergy, Asthma and Immunology; 1998;
[View In Article](#)
11. Ray NF, Baraniuk JN, Thamer M, et al. **Direct expenditures for the treatment of allergic rhinoconjunctivitis in 1996, including the contributions of related airway illnesses**. *J Allergy Clin Immunol*. 1999;103(pt 1):401-407
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(51 KB\)](#) | [CrossRef](#)
12. Halpern MT, Schmier JK, Richner R, Guo C, Toghias A. **Allergic rhinitis: a potential cause of increased asthma medication use, costs, and morbidity**. *J Asthma*. 2004;41:117-126
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
13. Thomas M, Kocovar VS, Zhang Q, Yin DD, Price D. **Asthma-related health care resource use among asthmatic children with and without concomitant allergic rhinitis**. *Pediatrics*. 2005;115:129-134
[View In Article](#)
14. Cox L, Li JT, Nelson H, Lockey R. **Allergen immunotherapy: a practice parameter second update**. *J Allergy Clin Immunol*. 2007;120:S25-S85
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(3387 KB\)](#) | [CrossRef](#)
15. Guilbert TW, Morgan WJ, Zeiger RS, et al. **Long-term inhaled corticosteroids in preschool children at high risk for asthma**. *N*

- Engl J Med.* 2006;354:1985–1997
[View In Article](#) | [CrossRef](#)
16. Durham SR, Walker SM, Varga EM, et al. Long-term clinical efficacy of grass-pollen immunotherapy. *N Engl J Med.* 1999;341:468–475
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 17. Hedlin G, Hellborn H, Lilja G, et al. Long-term follow-up of patients treated with a three-year course of cat or dog immunotherapy. *J Allergy Clin Immunol.* 1995;96(pt 1):879–885
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(600 KB\)](#) | [CrossRef](#)
 18. Jacobsen L, Nuchel Petersen B, Wihl JA, Lowenstein H, Ipsen H. Immunotherapy with partially purified and standardized tree pollen extracts, IV: results from long-term (6-year) follow-up. *Allergy.* 1997;52:914–920
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 19. Eng PA, Reinhold M, Gnehm HP. Long-term efficacy of preseasonal grass pollen immunotherapy in children. *Allergy.* 2002;57:306–312
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 20. Eng PA, Borer-Reinhold M, Heijnen IA, Gnehm HP. Twelve-year follow-up after discontinuation of preseasonal grass pollen immunotherapy in childhood. *Allergy.* 2006;61:198–201
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 21. Johnstone DE, Dutton A. The value of hyposensitization therapy for bronchial asthma in children: a 14-year study. *Pediatrics.* 1968;42:793–802
[View In Article](#) | [MEDLINE](#)
 22. Niggemann B, Jacobsen L, Dreborg S, et al. Five-year follow-up on the PAT study: specific immunotherapy and long-term prevention of asthma in children. *Allergy.* 2006;61:855–859
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 23. Novembre E, Galli E, Landi F, et al. Coseasonal sublingual immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis. *J Allergy Clin Immunol.* 2004;114:851–857
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(238 KB\)](#) | [CrossRef](#)
 24. Des Roches A, Paradis L, Menardo JL, Bouges S, Daures JP, Bousquet J. Immunotherapy with a standardized *Dermatophagoides pteronyssinus* extract, VI: specific immunotherapy prevents the onset of new sensitizations in children. *J Allergy Clin Immunol.* 1997;99:450–453
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(391 KB\)](#) | [CrossRef](#)
 25. Pajno GB, Barberio G, De Luca F, Morabito L, Parmiani S. Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy: a six-year follow-up study. *Clin Exp Allergy.* 2001;31:1392–1397
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 26. Hankin CS, Cox L, Eavy G, et al. Health economics of allergy immunotherapy. *Drug Benefit Trends.* 2008;20(suppl A):7–1320–21
[View In Article](#)
 27. Donahue JG, Greineder DK, Connor-Lacke L, Canning CF, Platt R. Utilization and cost of immunotherapy for allergic asthma and rhinitis. *Ann Allergy Asthma Immunol.* 1999;82:339–347
[View In Article](#) | [Abstract](#) | [Full-Text PDF \(301 KB\)](#) | [CrossRef](#)
 28. Hankin CS, Cox L, Lang D, et al. Allergy immunotherapy among Medicaid-enrolled children with allergic rhinitis: patterns of care, resource use, and costs. *J Allergy Clin Immunol.* 2008;121:227–232
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(177 KB\)](#) | [CrossRef](#)
 29. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed?. *BMJ.* 2000;320:1197–1200
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
 30. Berto P, Bassi M, Incorvaia C, et al. Cost effectiveness of sublingual immunotherapy in children with allergic rhinitis and asthma. *Allerg Immunol (Paris).* 2005;37:303–308
[View In Article](#) | [MEDLINE](#)
 31. Ariano R, Berto P, Tracci D, Incorvaia C, Frati F. Pharmacoeconomics of allergen immunotherapy compared with symptomatic drug treatment in patients with allergic rhinitis and asthma. *Allergy Asthma Proc.* 2006;27:159–163
[View In Article](#) | [MEDLINE](#)
 32. Fireman P. Therapeutic approaches to allergic rhinitis: treating the child. *J Clin Allergy Immunol.* 2000;105(pt 2):S616–S621
[View In Article](#)
 33. Arrighi HM, Maier WC, Redding GH, Morray BH, Llewellyn CE. The impact of allergic rhinitis in Seattle school children [abstract 208]. *J Clin Allergy Immunol.* 1995;95:192
[View In Article](#)
 34. Calderon M, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. *Cochrane Database Syst Rev.* 2007;(1):CD001936
[View In Article](#)

35. Moller C, Dreborg S, Ferdousi HA, et al. **Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study).** *J Allergy Clin Immunol.* 2002;109:251–256
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(162 KB\)](#) | [CrossRef](#)
36. Law AW, Reed SD, Sundy JS, Schulman KA. **Direct costs of allergic rhinitis in the United States: estimates from the 1996 Medical Expenditure Panel Survey.** *J Allergy Clin Immunol.* 2003;111:296–300
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(77 KB\)](#) | [CrossRef](#)
37. Nolte H, Nepper-Christensen S, Backer V. **Unawareness and undertreatment of asthma and allergic rhinitis in a general population.** *Respir Med.* 2006;100:354–362
[View In Article](#) | [Abstract](#) | [Full Text](#) | [Full-Text PDF \(174 KB\)](#) | [CrossRef](#)
38. Baptist AP, Baldwin JL. **Physician attitudes, opinions, and referral patterns: comparisons of those who have and have not taken an allergy/immunology rotation.** *Ann Allergy Asthma Immunol.* 2004;93:227–231
[View In Article](#) | [Abstract](#) | [Full-Text PDF \(158 KB\)](#) | [CrossRef](#)
39. Leatherman BD, Owen S, Parker M, et al. **Sublingual immunotherapy: past, present, paradigm for the future? (a review of the literature).** *Otolaryngol Head Neck Surg.* 2007;136(suppl):S1–S20
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
40. Cohn JR, Pizzi A. **Determinants of patient compliance with allergen immunotherapy.** *J Allergy Clin Immunol.* 1993;91:734–737
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)
41. Lower T, Henry J, Mandik L, Janosky J, Friday GA. **Compliance with allergen immunotherapy.** *Ann Allergy.* 1993;70:480–482
[View In Article](#) | [MEDLINE](#)
42. More DR, Hagan LL. **Factors affecting compliance with allergen immunotherapy at a military medical center.** *Ann Allergy Asthma Immunol.* 2002;88:391–394
[View In Article](#) | [Abstract](#) | [Full-Text PDF \(311 KB\)](#) | [CrossRef](#)
43. Nathan RA. **The burden of allergic rhinitis.** *Allergy Asthma Proc.* 2007;28:3–9
[View In Article](#) | [MEDLINE](#) | [CrossRef](#)

Disclosures: BioMedEcon LLC is a consultant to Greer Laboratories Inc.

Funding Sources: Funding for this research was provided by Greer Laboratories Inc.

PII: S1081-1206(09)00011-8

doi:10.1016/j.anai.2009.11.010

© 2010 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

[« Back](#)

Annals of Allergy, Asthma & Immunology
[Volume 104, Issue 1](#), Pages 79-85, January 2010

Copyright © 2011 Elsevier Inc. All rights reserved. | [Privacy Policy](#) | [Terms & Conditions](#) | [Feedback](#) | [About Us](#) | [Help](#) | [Contact Us](#)
The content on this site is intended for health professionals.

Advertisements on this site do not constitute a guarantee or endorsement by the journal, Association, or publisher of the quality or value of such product or of the claims made for it by its manufacturer.