Allergy immunotherapy among Medicaid-enrolled children with allergic rhinitis: Patterns of care, resource use, and costs

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Background: Although research demonstrates that allergy immunotherapy (IT) improves allergic rhinitis (AR) outcomes, little is known about IT patterns of care and associated resource use and costs among US children with diagnoses of AR.
Objective: We sought to examine characteristics associated with receiving IT, patterns of IT care, and health care use and costs incurred in the 6 months before versus after IT.
Methods: We performed retrospective Florida Medicaid claims data (1997-2004) analysis of children (<18 years of age) given new diagnoses of AR.
Results: Of 102,390 patients with new diagnoses of AR, 3048 (3.0%) received IT. Male patients, Hispanic patients, and those with concomitant asthma were significantly more likely to receive IT. Approximately 53% completed less than 1 year and 84% completed less than 3 years of IT. Patients who received IT used significantly less pharmacy (12.1 vs 8.9 claims, $P < .0001$), outpatient (30.7 vs 22.9 visits, $P < .0001$), and inpatient (1.2 vs 0.4 admissions, $P = .02$) resources in the 6 months after versus before IT. Pharmacy ($330 vs $60, $P < .0001$), outpatient ($735 vs $270, $P < .0001$), and inpatient ($2441 vs $1, $P < .0001$) costs (including costs for IT care) were significantly reduced after IT.
Conclusion: Despite suboptimal treatment persistence (only 16% of patients completed 3 years of IT), resource use and costs after treatment were significantly reduced from pre-IT levels.
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Key words: *Allergy, immunotherapy, allergic rhinitis, children, use, persistence, cost, Medicaid*

The effect of allergic rhinitis (AR) on pediatric health is often underappreciated,[1] despite the fact that allergies are the third most prevalent chronic disease among children in the United States[2] and that AR in children accounted for an estimated $2.3 billion in US health care costs in 1996.[3] Because AR increases the risk of childhood comorbidities, such as asthma, otitis media with effusion, sinusitis, and respiratory infections,[4] disease management strategies must aim not only to control symptoms but also to prevent long-term consequences.[5]

According to allergen immunotherapy practice parameters developed by the Joint Task Force of the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma and Immunology, management of AR in children can include allergen avoidance, pharmacologic treatments, and/or allergy immunotherapy (IT).[6] Typically, IT is reserved for individuals who do not sufficiently respond to allergen avoidance and pharmacotherapy, but IT also might be initiated for its potential to affect the course of disease by reducing symptoms and medication reliance on a long-term basis.[6] IT has been associated with a statistically significant reduction in the risk of new-onset asthma in children with AR[7-9] and the development of new allergies among children with AR, asthma, or both.[10-14] The clinical benefits of IT have been shown to persist for an additional 3 to 12 years after discontinuation of a 2.5- to 5-year treatment course.[9,10,12,13,15-20]

Despite compelling evidence of the clinical benefits of IT in childhood AR,[21,22] little is currently known about IT patterns of use and associated cost benefits among US children. Only 3 US published studies have reported rates of IT use,[23-25] and few reports have described adherence to IT regimens.[26-30] With 3 exceptions,[24-26] these studies reflect health care use that occurred 10 to 15 years ago, and the more recently completed studies have not included children with AR.

Six English-language studies evaluating the economic benefits of IT have been published,[23,31-35] of which only one was conducted in the United States[23] and only one focused exclusively on children.[32] Study comparisons are hampered by variable approaches to assessing costs; some retrospective claims analyses

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Abbreviations used
AR: Allergic rhinitis
ICD: International Statistical Classification of Diseases and Related Health Problems
IT: Allergy immunotherapy
OR: Odds ratio

omitted inpatient costs,[32,24] and others relied on patient or physician recall to evaluate health care resource use and costs.[31,33,35]

The present study was conducted to examine IT use, patterns of care, and associated direct medical costs among children with AR. Specifically, Medicaid claims data of children with AR were retrospectively analyzed to address 3 major objectives:

1. to determine demographic and comorbid allergy-related illness characteristics associated with receiving IT among children with new diagnoses of AR;
2. to examine patterns of IT care among patients who received *de novo* IT; and
3. to compare health (pharmacy, outpatient, and inpatient) services use and costs during the 6 months before IT initiation with those during the 6 months after discontinuation of IT.

METHODS

Florida Medicaid dataset

Florida Medicaid provides access to health care for more than 2 million low-income individuals, and more than half of 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) and Current Procedural Terminology diagnosis and treatments codes, and payment data. Information is patient deidentified and fully compliant with the Health Insurance Portability and Accountability Act Privacy Rule.

Definition of terms used in analyses

The presence of an AR diagnosis was identified by ICD-9 code 477.X. IT 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. Given that the Joint Task Force suggests that a conventional course of treatment is at least 3 years' duration, premature termination was characterized as IT administered for a period of less than 3 years.[6] Patients with new diagnoses of 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* IT if they had new diagnoses of AR and if their first documented IT claims followed (rather than preceded) newly diagnosed AR. The build-up phase of treatment was defined as the first 6 months after IT initiation; the maintenance phase was defined as IT occurring after the 6-month build-up phase.

Study sample

Subjects were selected from Florida Medicaid enrollees who had a paid claim from July 1997 through June 2004. Patients were identified according to the 3 major objectives of this study. To examine characteristics associated with receiving IT, all patients with new diagnoses of AR were selected. To examine patterns of *de novo* IT care, the sample was further narrowed to include only those patients who received *de novo* IT and who had at least 4 years of claims data after their index AR diagnosis. To compare all (including allergy-related and non–allergy-related) health care costs incurred during the 6-month period after IT discontinuation with costs incurred in the 6 months before IT initiation, the sample was further restricted to patients with at least 6 months of claims data after their final IT administration.

Data analyses

Datasets from July 1997 through June 2004 were provided by the Florida Medicaid Program in 21 files in compressed text format. These were decompressed and imported for analysis by using SAS/STAT statistical software version 7 (2006; SAS Institute Inc, Cary, NC). To address objective 1, *t* tests were used to compare continuous variables, and χ^2 tests were used for categorical variables. If the overall test was significant, additional analyses were conducted to compare subgroups. To address objective 3, cost data were logarithmically transformed to correct for the skewed data, and paired *t* tests were used to compare resource use and transformed costs during the 6 months before and 6 months after receiving IT. Because continuous variable data were not always normally distributed, Wilcoxon signed-rank tests were performed to confirm the results of *t* tests conducted on nontransformed means. Unless otherwise indicated, the results of nonparametric statistical testing were consistent with the results of parametric statistical tests.

Logistic regression was used to calculate likelihood estimates for variables associated with IT use, and Cox proportional hazard analysis was used to evaluate predictors of premature IT discontinuation.

RESULTS

Results of the sample identification procedures used to address objectives 1 to 3 are shown in Fig 1.

Objective 1: To determine demographic and comorbid allergy-related illness characteristics associated with receiving IT among children with new diagnoses of AR

Among 2,718,101 Medicaid-enrolled children, 124,755 were given diagnoses of AR, and 102,390 were given new diagnoses of AR during the index period. Among patients with new diagnoses of AR, 3.0% (3048) received IT during the 7-year study period. Table I presents the demographic and comorbid allergy-related illness characteristics for all patients with new diagnoses of AR and for those who did or did not receive IT. The mean age at first AR diagnosis of the total sample was 7.1 years (SD, 4.5 years).

Adjusting for the distribution of male and female children in the overall Medicaid dataset, the proportion of male patients with a diagnosis of AR was significantly greater than the proportion of female patients (odds ratio [OR], 1.09; 95% CI, 1.08-1.10; $P < .0001$). This highly statistically significant finding is likely attributable to the large sample size and might not reflect a clinically meaningful difference. This caveat might apply to other statistically significant findings in this section. Subsequent analyses, stratified by age group, indicated that whereas male patients less than 10 years of age were 11% more likely than female patients of similar age to have a diagnosis of AR (OR, 1.11; 95% CI, 1.09-1.12; $P < .0001$), male and female patients aged 10 to 18 years were equally likely to receive an AR diagnosis (OR, 0.98; 95% CI, 0.95-1.01; $P = .15$).

Adjusting for the race/ethnicity distribution of children in the overall Medicaid dataset, Hispanic patients were 16% more likely to have a diagnosis of AR than white patients (OR, 1.16; 95% CI, 1.14-1.17; $P < .0001$), 52% more likely to have an AR diagnosis than African American patients (OR, 1.52; 95% CI, 1.50-1.55; $P < .0001$), and 77% more likely to have an AR diagnosis than those of other races/ethnicities (OR, 1.77; 95% CI, 1.73-1.82; $P < .0001$).

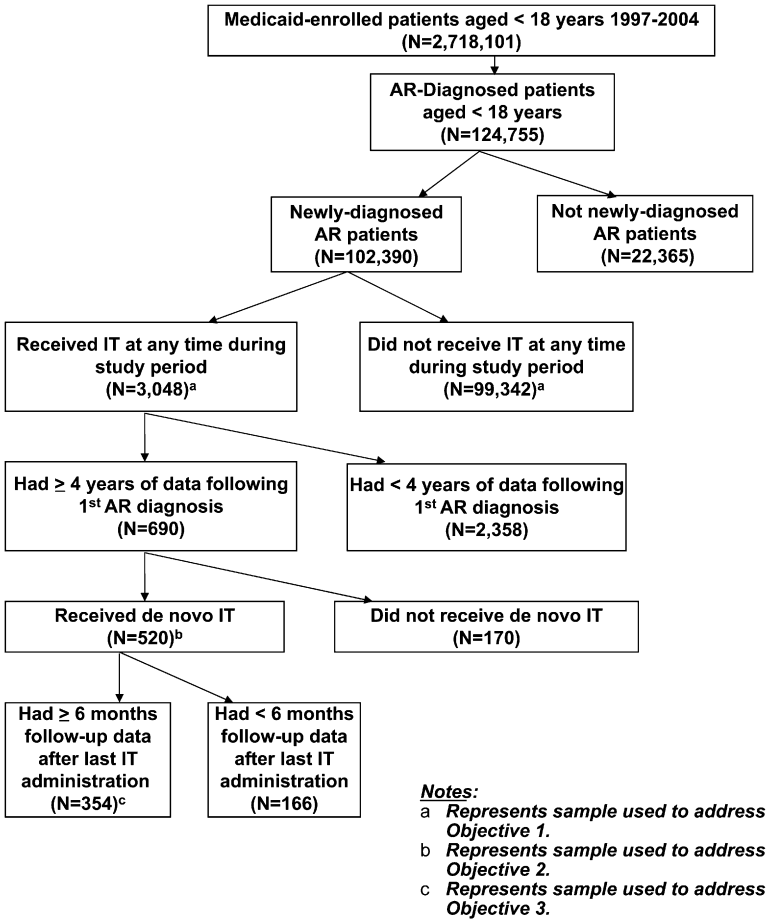

FIG 1. Results of the sample-identification procedure.

TABLE I. Characteristics of patients with new diagnoses of AR who received or did not receive IT

Characteristic	All Medicare patients <18 y (n = 2,718,101)	All patients with newly diagnosed AR (n = 102,390)	Patients receiving IT (n = 3048)	Patients not receiving IT (n = 99,342)	*P* value, IT vs no IT
Age (y) at first AR diagnosis, mean (SD)	NA	7.1 (4.5)	7.6 (3.6)	7.0 (4.5)	<.0001*
Sex					
Male (% [N])	50.9 (1,379,918)	52.9 (54,110)	58.1 (1771)	52.7 (52,339)	<.0001
Female (% [N])	49.1 (1,332,293)	47.1 (48,280)	41.9 (1277)	47.3 (47,003)	
Race/ethnicity					
White (% [N])	35.1 (953,732)	38.8 (39,721)	27.1 (827)	39.1 (38,894)	<.0001
African American (% [N])	30.4 (826,010)	25.5 (26,147)	19.6 (598)	25.7 (25,549)	
Hispanic (% [N])	24.1 (656,481)	30.1 (30,873)	46.4 (1414)	29.7 (29,459)	
Other (% [N])	10.4 (281,878)	5.5 (5649)	6.9 (209)	5.5 (5440)	
Comorbid allergy-related illness					
Asthma (% [N])	—	29.6 (30,341)	51.0 (1556)	29.0 (28,785)	<.0001
Atopic dermatitis (% [N])	—	5.8 (5994)	10.7 (327)	5.7 (5667)	<.0001
Conjunctivitis (% [N])		18.6 (19,312)	19.8 (604)	18.8 (18,708)	.1712

*P value was significant for both the Wilcoxon signed-rank test and t test.

There were significant sex and racial/ethnic differences between patients who did or did not receive IT after adjusting for differences in the likelihood of AR diagnosis. Male patients were 25% more likely to receive IT than female patients (OR, 1.25; 95% CI, 1.16-1.34; $P < .0001$), and Hispanic patients were 2.1 times more likely to receive IT than African American patients (OR, 2.05; 95% CI, 1.86-2.26; $P < .0001$) and 2.3 times more likely to receive IT than white patients (OR, 2.26; 95% CI, 2.07-2.46; $P < .0001$).

Patients who received IT were older at first AR diagnosis than those who did not receive IT (mean, 7.6 vs 7.0 years; $P < .0001$).

Patients who were given diagnoses of comorbid asthma were 2.6 times more likely to receive IT than their counterparts without asthma (OR, 2.564; 95% CI, 2.38-2.75; $P < .0001$), and those with comorbid atopic dermatitis were nearly twice as likely to receive IT than those without this skin condition (OR, 1.99; 95% CI, 1.77-2.23; $P < .0001$). Comorbid conjunctivitis was not related to the likelihood of IT initiation (OR, 1.06; 95% CI, 0.97-1.17; $P = .17$).

Objective 2: To examine patterns of IT care among patients who received *de novo* IT

There were 520 patients with new diagnoses of AR who received *de novo* IT and had at least 4 years of claims data after their index AR diagnosis (Fig 1).

Age at IT initiation. At IT initiation, the mean age was 8.2 years (SD, 3.1 years). Approximately 12% of patients were less than 5 years of age, 63% were 5 to 10 years of age, and 25% were 11 years of age or older.

Time from first AR diagnosis to IT initiation. On average, there were approximately 1.5 years (543 days [SD, 571 days]) between the first AR diagnosis and IT initiation. Compared with white patients, those of other racial/ethnic groups were 2.9 times more likely to initiate IT within 6 months of their first AR diagnosis (OR, 2.94; 95% CI, 1.4-6.2; $P = .0049$).

IT regimen. Among all patients who had at least 2 IT administrations, the average number of days between administrations was 27.2 (SD, 68.8 days; range, 1-1117 days). During the build-up phase of treatment, the average number of days between IT administrations was 16.2 (SD, 17.5 days; range, 1-171 days); 33.8% of patients received injections, on average, more than 2 weeks apart. During the maintenance phase of treatment, the average number of days between IT administrations was 24.9 (SD, 31.8 days; range, 1-363 days); 9.7% received injections, on average, more than 6 weeks apart.

Duration of IT. Patients received an average of 31.3 IT administrations (SD, 34.3 administrations). The mean duration of treatment was 17 months (SD, 17.6 months). Approximately 39% (n = 202) of patients received IT for less than 6 months, 14% (n = 73) for at least 6 months but less than 1 year, 18% (n = 96) for at least 1 year but less than 2 years, 13% (n = 66) for at least 2 years but less than 3 years, and 16% (n = 83) for 3 or more years.

Hispanic patients received significantly ($P = .003$) shorter courses of therapy (mean, 429 days [SD, 467 days]) than did white patients (mean, 613 days [SD, 571 days]), African American patients (mean, 559 days [SD, 593 days]), or patients of other races/ethnicities (mean, 659 days [SD, 624 days]). Hispanic patients were 1.5 times more likely to discontinue IT within 2 years than white patients (Cox proportional hazard = 1.53, $P = .001$).

Objective 3: To compare health services use (pharmacy, outpatient, and inpatient) and costs during the 6 months before IT initiation with those during the 6 months after discontinuation of IT

Table II shows health services use and costs during the 6 months before IT initiation and the 6 months after IT termination. There was a significant reduction in the mean number of pharmacy claims, outpatient visits, and hospital admissions and associated costs of these services from before IT to after IT. The mean cost per IT administration was $20 (SD, $23), and the total mean cost of IT was $424 (SD, $453). The average 6-month weighted cost savings per patient was $401.

DISCUSSION

Despite suboptimal treatment persistence, patients who received IT realized significant reductions in health care resource use and costs in the 6 months before versus after IT. Given that at least 3 years of IT are generally recommended to achieve persistent clinical benefit,[6] we were surprised to find that these results were robust across all health care use, including pharmacy, outpatient, and inpatient services. Moreover, the average 6-month savings in health care costs ($401 per patient) was sufficient to offset the average total cost of IT across the course of therapy ($424 per patient).

The 3% use rate we report among Medicaid-enrolled children given new diagnoses of AR is consistent with IT use rates reported in other population-based analyses.[23,36] Because of the nature of administrative claims data, we are unable to determine whether this 3% rate reflects appropriate use or indicates undertreatment. Our findings provide support for the contention that administration of IT to appropriate patients with AR is associated with reduced health care use and cost savings. Additional benefit might be realized when treatment adherence and persistence improve.

The 84% premature termination rate found in the present study is the largest reported to date. Previous studies have reported rates ranging from less than 25% to 67%.[23,26-30] Inconsistencies can be attributable to different populations (eg, military personnel and family members,[26] children only,[28] adults only,[27] and adults and children[23,29,30]), treatment sites (eg, private practice settings,[23,29,30] military medical center,[26] children's medical center,[28] and university-based hospital[27]), and definitions of premature termination (eg, not receiving an IT injection in the past 3 months unless directed by an allergist or completed 5 years of treatment[26]; stopping IT without physician permission[29]; not receiving an IT injection within the past 6 months[27,28]; receiving $\geq$20 IT injections in the first 6 months, $\geq$30 injections during the first year, >31 injections over the next 2.5 years, and $\geq$61 injections over 3.5 years[23]; and stopping IT before completing 3 years of treatment[30]) used across studies.

In the present study boys younger than 10 years were significantly more likely to be given diagnoses of AR than girls of the same age, whereas there was no sex difference among older children. Similar variation in AR diagnosis by sex and age has been reported previously.[37-39] We also found that after controlling for variation in AR diagnosis by sex, boys were significantly more likely to receive IT than girls. To our knowledge, this is the first report of a disparity in AR treatment by sex.

We found variations in health care use based on race and ethnicity. Whereas Hispanic patients were significantly more likely to receive a diagnosis of AR and to receive IT than other racial or ethnic groups, they also were significantly more likely to prematurely terminate treatment. These results invite further exploration of cultural barriers to IT persistence.[40]

Our findings suggest that IT is associated with reductions in health care costs. This is in contrast to the results of a previous retrospective claims analysis of US adults and children[23] but is consistent with findings of a retrospective analysis of medical records among Italian children.[32] The US study found that patients who completed 3.5 years of IT had 55% higher medical costs compared with patients who completed IT of shorter duration.[23] However, those who completed 3.5 years of IT also had 30% higher medical

TABLE II. Change in health services use and health care costs for patients with AR diagnoses who received IT

	Patients with AR diagnoses who received IT (n = 354)				
	No. of subjects	No. of claims/cost during 6 mo before IT	No. of claims/cost during 6 mo after IT	Change in no. of claims/cost*	*P* value†
Health services use per patient, mean (SD)‡					
Pharmacy claims	339	12.1 (9.4)	8.9 (11.4)	−3.2	<.0001
Outpatient visits	352	30.7 (32.1)	22.9 (31.1)	−7.8	<.0001
Hospital admissions	18	1.2 (0.4)	0.4 (1.0)	−0.8	.02
Health care costs per patient, mean (SD)§					
Pharmacy cost					
Arithmetic mean (SD)	339	$566 ($1033)	$512 ($1081)	$−54 (−$112 to $−45)	
Geometric mean (SD)	339	$330 ($2.70)	$60 ($30)	$0.18 (0.12 to 0.25)	<.0001
Outpatient cost					
Arithmetic mean (SD)	352	$1149 ($1759)	$916 ($2041)	−$233 (−$381 to −$84)	
Geometric mean (SD)	352	$735 ($2.5)	$270 ($7.4)	$0.37 (0.30 to 0.45)	<.0001
Inpatient cost					
Arithmetic mean (SD)	18	$3061 ($2068)	$744 ($1739)	−$2316 (−$3800 to −$832)	
Geometric mean (SD)	18	$2441 ($2)	$1 ($60)	2×10^{-4} (3×10^{-5} to 2×10^{-3})	<.0001
Total cost					
Arithmetic mean (SD)	354	$1850 ($2354)	$1635 ($3525)	−$215 (−$470 to $40)	
Geometric mean (SD)	354	$1212 ($2.2)	$493 ($8.2)	$0.41 (0.33 to 0.50)	<.0001
Weighted cost‖	354		(339 × $54) + (352 × $233) + (18 × $2316)/354 = $401		

*Differences between pre- and post-IT costs were calculated by using the mean difference score for arithmetic means and the ratio of geometric means for geometric means. 95% CIs are shown in parentheses.

†*P* values were based on *t* tests comparing number of claims and log transformed mean costs. Wilcoxon signed-rank test results confirmed results of *t* tests comparing number of claims.

‡Health services use includes allergy-related and non–allergy-related health care.

§Includes costs for IT care (pharmacy and outpatient visits).

‖Weighted cost based on arithmetic mean.

costs during the year before starting IT, suggesting a higher disease burden and confounding interpretation of group differences. Methods used in the Italian study were more similar to ours.

This study had several limitations. First, results based on Medicaid enrollees might not be generalizable to privately insured or higher-income patients. Second, study results were limited to children younger than 18 years and might not apply to adults. Third, the nature of available claims data did not allow us to examine the contribution of potentially important variables, such as the number and specific types of AR diagnoses (eg, seasonal or perennial), the types of settings in which patients received their IT treatment (eg, hospital, allergy specialist clinic, and primary care office), reasons for discontinuing treatment, and responses to previous treatments. Fourth, because health care resource use and cost follow-up data were limited to 6 months after IT termination, long-term cost benefits associated with IT remain unknown. Because most patients in our study were unlikely to experience sustained clinical benefits after IT (because of premature termination), cost savings realized in the first 6 months after IT might attenuate over a longer follow-up period. Fifth, it is possible that reductions in health care resource use and costs observed in this uncontrolled study were due to factors other than the effects of IT, such as the increase in monitoring and care given to patients who received IT. Another possibility is that the initiation of IT was prompted by patients reaching a peak disease state and that subsequent reductions in health care use were the result of a natural waning of disease severity rather than an effect of treatment. Although this cannot be definitively ruled out, longitudinal research suggests that some patients might experience a waning of symptoms, although only after having AR for several decades,[41] and that a significant proportion of untreated children will experience disease progression during childhood, as evidenced by the development of new sensitivities[12-14,42] and comorbid asthma.[8,9,43] Sixth, because only a small subset of patients with new diagnoses of AR initiated IT, this group of patients might differ from the overall population of children with diagnoses of AR. In fact, our data suggest that these patients were more severely ill (given their greater likelihood of comorbid asthma and atopic dermatitis) than patients who did not initiate IT. Finally, we could not determine the point at which IT became cost saving because too few patients in our sample completed sufficient treatment duration.

Despite high rates of premature discontinuation, we found that patients with AR who received IT realized significant reductions in health care resource use and costs in the 6 months after IT discontinuation compared with the 6 months preceding IT initiation.

In the United States IT is commonly delivered as a clinician-administered subcutaneous injection. As such, IT presents substantial barriers to access, continuity, and persistency of care. In contrast to the United States, oral sublingual allergen immunotherapy is prescribed in Europe and is generally self-administered at home. Sublingual allergen immunotherapy has been associated with a higher persistency rate than observed in this and previous studies of patients receiving subcutaneous allergen immunotherapy.[11,44] Findings suggest that such innovations in IT delivery might lead to improved adherence and associated outcomes of care among patients who receive IT for AR.

Although prospective, longitudinal, randomized controlled trials specifically designed to assess the cost-effectiveness of IT

are needed, retrospective analysis of claims data is a valuable tool for determining the economic effect of IT in the real world because results are less influenced by careful patient selection, tracking, and rigorous follow-up. We found significant reductions in health care use and costs after IT, despite suboptimal treatment persistence. These findings are encouraging and constitute a first step toward establishing the cost benefits of IT among US patients.

Clinical implications: This is the first study to report substantial short-term cost offsets among patients with AR diagnoses who received IT, although the majority did not complete sufficient treatment duration to experience full potential benefit. Findings suggest that improved access and increased treatment persistence might yield even greater benefits.

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