

Real-world mapping of allergy immunotherapy in the United States: The argument for improving adherence

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ABSTRACT

Background: There is a dearth of real-world evidence studies focused on allergy immunotherapy (AIT) use among patients with allergic rhinitis (AR).

Objective: This study examined claims data of AR patients residing in the United States to assess patient characteristics and health outcomes.

Methods: AR patients were identified in the IBM MarketScan database between January 1, 2014, and March 31, 2017. Patients receiving AIT were identified with relevant billing codes (earliest AIT claim for vaccine as the index date); patients without AIT were identified with claims that contained a diagnosis code for AR (earliest AR claim as the index date). All the patients were required to have continuous enrollment 12 months prior to and following their index date. AIT patients reaching 25+ injection claims were analyzed as a separate maintenance cohort. Patients were assessed for demographic characteristics, comorbid conditions, and health care utilization.

Results: A total of 2,334,530 AR patients were included; 103,207 had at least one AIT claim, with 45,279 (43.9%) of these patients reaching maintenance. Patients who reached AIT maintenance presented higher rates of baseline comorbidities than both the full AIT cohort and the patients with no AIT claims, including asthma (34.6% versus 30.1% versus 7.5%) and upper respiratory tract infections (63.1% versus 60.3% versus 34.2%). From baseline to follow-up, maintenance AIT patients demonstrated reductions in all AR-related comorbidities assessed, along with reductions in all-cause and AR-related service utilization.

Conclusion: Patients initiating AIT presented the greatest need for therapeutic intervention, as evidenced by higher allergy-related comorbidities; those who reached maintenance demonstrated improved outcomes following the initiation of therapy. Continued efforts to increase patient awareness and adherence to AIT are needed.

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The prevalence of allergic diseases has increased worldwide over the past 50 years, with sensitization rates to common allergens approaching 50% in school-age children.¹ Allergic rhinitis (AR), an inflammatory process stimulated by environmental allergens and characterized by sneezing, watery, and itchy eyes,² has been shown to affect 10–30% of the world population, with ~17.6 million adults diagnosed with AR in 2012 in the United States.³ Quality of life and work productivity have both been shown to be affected by the presence of AR one in three patients

report impairment on the job, with a direct relationship to symptom severity.^{4,5} Thus, the economic impact of AR is significant, with estimates of medical costs at nearly \$3.4 billion annually.⁶ The presence of either seasonal or perennial AR will increase the probability of asthma.^{7,8} Atopic eczema and allergic conjunctivitis are also common comorbidities with AR, with atopic eczema potentially preceding AR.^{9,10} Further, patients with AR have also been shown to be twice as likely to develop problems sleeping.¹¹ As such, AR is seldom an isolated disorder, and the associated sequelae common to many patients should be taken into consideration when assessing the true burden of this disease.

Three options are typically reviewed when considering a disease management approach: avoidance, pharmacotherapy, and immunotherapy.¹² Though pharmacotherapy can suppress symptoms of AR, allergy immunotherapy (AIT) is the only therapy that can modify the underlying course of the disease.¹³ AIT is typically used for the most severe patients and can be delivered *via* subcutaneous and sublingual routes, with tablets being U.S. Food and Drug Administration approved for the latter route.

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Recently published AIT clinical practice guidelines emphasize the importance of adherence monitoring *via* patient education and appointment reminders to promote treatment compliance, along with the incorporation of shared decision making into the discussion of any treatment plan.¹⁴ Real-world evidence studies have shown an economic benefit associated with AIT in the treatment of AR,^{15,16} but limited evidence exist for AIT utilization treatment patterns and health care service use profiles of AR patients, particularly those who receive AIT. Therefore, the purpose of this exploratory study was to better understand the current patient and treatment landscape of AR in the United States. Patient comorbidity profiles, treatment patterns, and health care service utilization were assessed, with a focus on patients receiving AIT.

METHODS

Study Design and Data Source

This observational, retrospective study used de-identified health care claims from the IBM (IBM Corp., Armonk, New York, USA) MarketScan Commercial Database spanning January 1, 2014, through March 31, 2017. The data base comprises inpatient medical, outpatient medical, and outpatient pharmacy claims data, along with enrollment and demographic information, collected from employees, dependents, retirees, and members of >300 large self-insured U.S. employers and >25 U.S. health plans. All data base records were de-identified and fully compliant with the U.S. Health Insurance Portability and Accountability Act (HIPAA); this compliance with HIPAA regulation meant that patient consent and Institutional Review Board approval to conduct this study were unnecessary.

Patient Selection and Cohort Assignment

Study inclusion criteria were as follows:

- The presence of ≥ 1 medical or pharmacy claims for AIT and, if an absence of AIT claims, ≥ 1 claim with a diagnosis of AR (*International Classification of Diseases, Ninth Revision - Clinical Modification* code 477.x or *International Classification of Diseases, Tenth Revision - Clinical Modification* code J30.x) between January 1, 2014, and March 31, 2017.
- The earliest service date for either an AIT or AR claim served as the index date.
- At least 12 months of continuous enrollment with medical and pharmacy benefits for 12 months preceding and following the index dates.

For the patients in the AIT cohort, the 12-month pre-index period was required to be absent of any AIT treatment, and patients were excluded if they presented any claims for venom allergies at any time

during the measurement window. AIT patients reaching the maintenance phase of treatment, operationally defined as presenting 25 + AIT injection claims, were analyzed as a stand-alone cohort. As the buildup phase of subcutaneous immunotherapy (SCIT) entails 1–2 shots per week for 3–6 months, the frequency of patients meeting this conservative threshold corresponded to a once-weekly shot regimen for 6 months was deemed an appropriate threshold.

MEASURES

Sample Characteristics

Patient demographic characteristics were assessed on the index date and included age, sex, geographic region, urbanicity, and the index year. Clinical characteristics were assessed during both the 12-month baseline and the follow-up periods, and included the Deyo-Charlson comorbidity index,¹⁷ the presence of comorbid conditions of interest (Table 3); use of specific prescription medication classes, including antihistamines, decongestants, intranasal corticosteroids, and nasal sprays; and the frequency of specific surgeries (polypectomy, septoplasty, sinus surgery, turbinectomy, and tympanostomy).

Outcomes

The total number of AIT and AIT injection-specific claims were assessed during the follow-up year, with the latter being used to identify AIT patients who successfully reached the maintenance phase of treatment. A gap of 90 days in treatment was used to define treatment discontinuation. All-cause and AR-specific health care resource utilization were assessed during each the 12-month baseline and the follow-up periods. AR-related resource use included all inpatient medical claims with any of the following diagnosis codes in the primary position or any position on outpatient claims: AR, asthma, atopic dermatitis, conjunctivitis, eosinophilic esophagitis, eustachian tube disorder, food allergy, headache, migraine, otitis media, skin rash (including pruritus), eczema, sleep apnea, sleep disturbance, bronchitis, any upper respiratory tract infection, nasal polyps, or chronic sinusitis. Additionally, all pharmacy claims indicated for AR or AR-related treatment, and any of the five surgeries listed above also contributed to disease-related utilization.

Statistical Analysis

Descriptive statistics were reported for demographics, clinical characteristics, and all outcome measures for three cohorts: all AIT patients, AIT patients reaching the maintenance phase of treatment, and non-AIT patients. Continuous variables were summarized using means and standard deviations (SD). Categorical variables were reported by using counts and percentages. As this was a

descriptive exploratory study, hypothesis testing was not conducted.

RESULTS

A total of 2,334,530 AR patients qualified for the study; 103,207 patients presented ≥ 1 AIT claim (either for preparation or administration), with 45,279 (43.9%) of AIT patients presenting 25+ AIT injection claims. The remaining 2,231,323 patients did not present AIT claims. Of 103,207 AIT patients, 24,640 (23.9%) never presented a single injection claim, with 17.2% showing just a single claim of any type (injection or noninjection [e.g., preparation and provision]), and 6.9% only showing a single injection claim (Table 1).

Groups were similar demographically, with mean patient ages in the early 30s, a slight majority of female patients, and residency primarily focused in urban areas of southern United States (Table 2). During the baseline year, discordant rates of a variety of comorbid conditions were observed between AIT and non-AIT cohorts, with AIT patients more likely to present claims for asthma (30.1% versus 7.5%), atopic dermatitis (7.1% versus 2.7%), and conjunctivitis (21.7% versus 4.4%) (Table 3). Additionally, prior to the initiation of treatment, AIT patients were more likely to fill prescription antihistamines (16.8% versus 4.7%), decongestants (28.9% versus 6.2%), nasal sprays (44.3% versus 11.1%), and intranasal corticosteroids (36.9% versus 11.3%), and also present an AR-related surgical procedure (4.1% versus 0.9%) compared to non-AIT patients. During the 12-month follow-up, AIT patients who reached the maintenance phase of treatment presented decreased rates of claims for all allergy-related comorbidities assessed compared to observed rates during the baseline period, including eczema (–41%), chronic cough (–24%), and sinusitis (–20%), while non-AIT patients presented increases (Fig. 1).

All-cause health care utilization during the follow-up period was similar for most service categories between AIT and non-AIT cohorts, though patients in the non-AIT cohort tended to present fewer total visits/prescriptions than AIT cohorts (Table 4). AIT patients were more likely to visit a specialist compared to non-AIT patients (58.7% versus 26.3%), and also were more likely to have a surgical procedure (4.1% versus 2.2%) (Table 4). Patients reaching the maintenance phase of AIT presented the highest rate of specialist visits, at 76.6%, though compared to the overall AIT cohort, presented lower rates of hospitalizations (2.4% versus 3.8%) and emergency room visits (19.3% versus 23.0%). Regarding AR-related service utilization, maintenance AIT patients presented lower ER visits compared to the full AIT and non-AIT cohorts (8.1% versus 9.6% and 9.3%) but greater pharmacy use (83.1% versus 77.6% and 63.4%) (Table 5).

Table 1 AIT claim distribution

No. Claims	Any AIT Claims (n = 103,207), % (n)	Injection Claims (n = 78,567), % (n)
1	100 (103,207)	100 (78,567)
2	83 (85,450)	91 (71,459)
5	70 (71,784)	83 (65,404)
10	60 (62,356)	75 (58,834)
25	47 (48,111)	58 (45,279)

AIT = Allergy immunotherapy.

From baseline to follow-up, however, AIT maintenance patients presented the largest decreases in service use categories assessed, which spanned both all-cause and AR-related utilization, with the exception of “other” outpatient services where consultations for AIT injections are included (Fig. 2). Results included reductions in the use of AR-related pharmacotherapy among the patients reaching the maintenance phase of treatment, specifically antihistamines (–6%), intranasal corticosteroids (–20%), and nasal sprays (–20%). As can be viewed in Fig. 2, the decline in overall, all-cause service utilization was primarily driven by reductions in AR-related services. Non-AIT patients presented increases in the majority of categories assessed from baseline to follow-up.

DISCUSSION

This study presents a real-world examination, of the comorbidity profiles, AIT treatment patterns, and health care service utilization rates of patients diagnosed with AR in the United States. Despite being introduced as a therapeutic option more than a century ago,¹⁸ patients continue to underutilize AIT, with < 5% of the current AR sample initiating this treatment, and less than half of these patients reaching the maintenance phase of treatment. Overall, AIT patients did present notably higher baseline rates of a variety of comorbid, allergy-related disorders compared to non-AIT patients, suggesting that patients most severely impacted by allergy and associated comorbidities were most likely to initiate AIT. However, from baseline to follow-up, patients who persisted with AIT treatment demonstrated notable reductions in all AR-related comorbidities assessed, along with reductions in service utilization across the primary places of service.

AIT patients were observed to present fairly progressed disease at the time of AIT initiation, evidenced by their increased levels of both allergy-related comorbidities and prescription-strength medications indicated for allergies. AIT remains an effective treatment option for this population, as among those reaching the maintenance phase, the proportion presenting claims for nearly all related comorbidities assessed

Table 2 Demographics by AIT cohorts

	≥25 AIT Fills (<i>n</i> = 45,279)	Any AIT Fills (<i>n</i> = 103,207)	No AIT Fills (<i>n</i> = 2,231,323)
Age, mean ± SD, y	33.2 ± 18.0	34.2 ± 17.3	32.0 ± 19.2
Age categories, <i>n</i> (%)			
<5 y	633 (1.4)	1604 (1.6)	185,838 (8.3)
5–11 y	7417 (16.4)	12,867 (12.5)	288,589 (12.9)
12–17 y	5,231 (11.6)	10,609 (10.3)	202,743 (9.1)
18–65 y	31,998 (70.7)	78,127 (75.7)	1,554,153 (69.7)
>65 y	0 (0.0)	0 (0.0)	0 (0.0)
Age categories, <i>n</i> (%)			
18–27	4269 (9.4)	12,357 (12.0)	263,302 (11.8)
28–37	6848 (15.1)	16,885 (16.4)	308,516 (13.8)
38–47	8574 (18.9)	20,925 (20.3)	361,546 (16.2)
48–57	8001 (17.7)	18,564 (18.0)	394,717 (17.7)
58–65	4306 (9.5)	9396 (9.1)	226,072 (10.1)
Sex, <i>n</i> (%)			
Male	20,004 (44.2)	43,162 (41.8)	973,797 (43.6)
Female	25,275 (55.8)	60,045 (58.2)	1,257,526 (56.4)
Geographic region, <i>n</i> (%)			
Northeast	6751 (14.9)	14,107 (13.7)	330,536 (14.8)
North central	8198 (18.1)	15,357 (14.9)	384,770 (17.2)
South	23,725 (52.4)	58,137 (56.3)	1,186,081 (53.2)
West	6431 (14.2)	15,088 (14.6)	319,442 (14.3)
Unknown	174 (0.4)	518 (0.5)	10,494 (0.5)
Insurance plan type, <i>n</i> (%)			
Comprehensive/indemnity	791 (1.7)	1943 (1.9)	55,766 (2.5)
Exclusive provider; organiza- tion/preferred provider; organization	27,371 (60.4)	61,651 (59.7)	1,328,617 (59.5)
Point of service	2699 (6.0)	6715 (6.5)	148,716 (6.7)
Health maintenance organization	4435 (9.8)	11,694 (11.3)	220,798 (9.9)
Consumer directed health plan/high deductible health plan	9553 (21.1)	20,153 (19.5)	439,360 (19.7)
Unknown	430 (0.9)	1051 (1.0)	38,066 (1.7)
Population density, <i>n</i> (%)			
Urban	40,055 (88.5)	90,275 (87.5)	1,948,820 (87.3)
Rural	5051 (11.2)	12,440 (12.1)	272,742 (12.2)
Unknown	173 (0.4)	492 (0.5)	9761 (0.4)
Index year, <i>n</i> (%)			
2014	14,009 (30.9)	33,157 (32.1)	727,487 (32.6)
2015	14,366 (31.7)	33,317 (32.3)	736,087 (33.0)
2016	13,657 (30.2)	29,777 (28.9)	602,157 (27.0)
2017	3247 (7.2)	6956 (6.7)	165,592 (7.4)

AIT = Allergy immunotherapy; SD = standard deviation.

during the postperiod were notably reduced from the baseline period (eczema, –41%; chronic cough, –24%; sinusitis, –20%); regarding the decrease in eczema, previous studies support the potential effectiveness of AIT as a treatment for atopic conditions.^{19–21} As such,

patients may benefit from initiating therapy sooner, which could function to curtail the development of a more severe disease and minimize the onset of additional allergy-related comorbidities. However, the benefit of any therapy can only be achieved if adherence

Table 3 Baseline clinical characteristics by AIT cohorts

	≥25 AIT Administrations (n = 45,279)	Any AIT Administrations (n = 103,207)	No AIT Administrations (n = 2,231,323)
Deyo-Charlson Comorbidity index score, mean ± SD	0.46 ± 0.72	0.45 ± 0.76	0.22 ± 0.66
Comorbid conditions of interest, n (%)			
Any upper respiratory tract infection	28,568 (63.1)	62,229 (60.3)	762,433 (34.2)
Sinusitis	19,291 (42.6)	41,897 (40.6)	385,113 (17.3)
Asthma	15,689 (34.6)	31,031 (30.1)	166,674 (7.5)
Conjunctivitis	12,277 (27.1)	22,372 (21.7)	98,447 (4.4)
Chronic cough	12,074 (26.7)	25,033 (24.3)	230,975 (10.4)
Upper respiratory tract infection	11,631 (25.7)	25,969 (25.2)	405,578 (18.2)
Chronic sinusitis	11,087 (24.5)	23,365 (22.6)	108,380 (4.9)
Heartburn, reflux, GERD	5748 (12.7)	13,346 (12.9)	143,469 (6.4)
Headache	5119 (11.3)	12,928 (12.5)	117,204 (5.3)
Otitis media	4980 (11.0)	10,287 (10.0)	196,258 (8.8)
Food allergy*	4503 (9.9)	9181 (8.9)	20,955 (0.9)
Bronchitis	4347 (9.6)	9851 (9.5)	116,626 (5.2)
Atopic dermatitis	3715 (8.2)	7324 (7.1)	59,502 (2.7)
Depression	3628 (8.0)	9473 (9.2)	126,999 (5.7)
Eczema	3469 (7.7)	7517 (7.3)	83,330 (3.7)
Sleep apnea	3365 (7.4)	7662 (7.4)	82,031 (3.7)
Eustachian tube disorder	3162 (7.0)	6660 (6.5)	49,032 (2.2)
Skin rash (including pruritus)	2634 (5.8)	6488 (6.3)	72,505 (3.2)
Sleep disturbance#	2594 (5.7)	6682 (6.5)	79,540 (3.6)
Migraine	2428 (5.4)	6243 (6.0)	61,997 (2.8)
Pneumonia	1313 (2.9)	2754 (2.7)	39,751 (1.8)
Nasal polyps	1295 (2.9)	2685 (2.6)	4970 (0.2)
Chronic tonsillitis	414 (0.9)	985 (1.0)	7387 (0.3)
Concomitant therapy, n (%)			
Nasal spray	23,653 (52.2)	45,766 (44.3)	246,566 (11.1)
Intranasal corticosteroid	19,435 (42.9)	38,058 (36.9)	251,121 (11.3)
Decongestant	13,626 (30.1)	29,796 (28.9)	139,088 (6.2)
Antihistamine	8155 (18.0)	17,371 (16.8)	105,286 (4.7)
Surgical procedures, n (%)§	2030 (4.5)	4239 (4.1)	20,195 (0.9)

AIT = Allergy immunotherapy; SD = standard deviation; GERD = gastroesophageal reflux disease.

*Includes peanuts, milk and milk produces, eggs, seafoods, and adverse symptoms related to food contact.

#Includes insomnia, hypersomnia, circadian rhythm sleep disorders, and narcolepsy.

§Include turbinectomy, endoscopic sinus surgery, septoplasty, tympanostomy, and nasal polypectomy.

and persistence to the therapeutic regimen is maintained. Improving disease control will result in a better quality of life, a reduction in health care utilization, and, ultimately, reduced health care expenditure; as the U.S. health care system has been shifting toward value-based care, increasing medication adherence and persistence have become paramount.²²

Though studies of AIT adherence have consistently reported rates around 50%,^{23–26} the observation in the current study that only 43.9% reached the maintenance phase of treatment after 12 months is disconcerting as most investigations of AIT include

multiple years of follow-up. Patients may need to persist with SCIT treatment for at least 12 months before realizing any therapeutic benefit²⁷ and potentially as much as 3 years to realize clinical remission among AR patients.²⁸ Though there is a wide range of reported adherence rates to a variety of chronic conditions,^{29–31} systemic reactions to SCIT are low (for a review, see James and Bernstein³²) and few patients report medication-related factors as reasons for SCIT non-adherence.³³

Inconvenience has historically been one of the primary drivers of SCIT non-adherence, due both to the

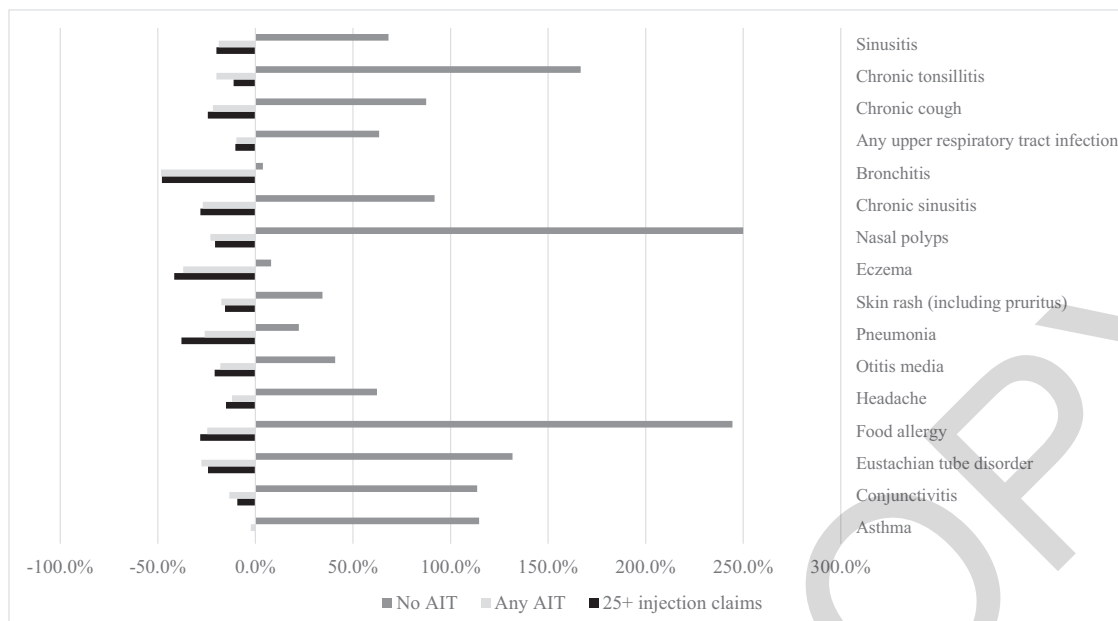


Figure 1. Allergic rhinitis-related comorbidities: Percentage change from baseline to post-index period.

frequency of visits for injections and the recommended duration of the AIT schedule,³³ though insurance coverage, cost, unrealistic expectations about the duration of therapy, and perceived ineffectiveness may also be drivers.^{34–38} Future efforts should continue to focus on methods to increase medication adherence and persistence, particularly through use of digital technology as there is some evidence that these types of interventions can improve adherence among AR patients receiving SCIT³⁹ and also among certain patients who are receiving medications for the management of asthma.⁴⁰ Though such interventions may not be suitable for all patients,^{41,42} the goal of increased adherence remains and can lead to improved long-term outcomes.⁴³ Certainly, sublingual immunotherapy (SLIT) tablets (the only U.S. Food and Drug Administration option in the United States) may present a better option to promote adherence for some proportion of the AR population, given their inherent convenience when compared with allergy shots.

The present findings also suggest that shared decision making in the management of AR, defined as a clinical approach in which the patient and the provider share in the decision when selecting a treatment path,⁴⁴ is warranted. As AIT can be a demanding treatment option, it is critical that patients are fully aware of the necessary commitment to fully benefit from this therapy. A recent analysis has demonstrated the beneficial impact of shared decision making on AIT use and adherence,³⁷ and Steven⁴⁵ recently published an overview highlighting reasons for shared decision making within the AR treatment paradigm, emphasizing the changing nature of the disease, patients'

tendencies to self-medicate, and education about the long-term goals of AIT in particular.⁴⁵

The Allergies, Immunotherapy, and Rhinoconjunctivitis (AIRS) survey revealed significant discrepancies between patient and provider perceptions of AIT,^{46,47} highlighting a concerning disconnect between the two. A number of shared decision making tools have become available in recent years for the allergy health care provider (for a review, see Blaiss *et al.*⁴⁸), including one developed by the American College of Allergy, Asthma, and Immunology focused on AIT. Also related to treatment outcomes, route of administration and treatment schedules have also been shown to impact the likelihood of treatment initiation, as a recent study demonstrated that 46% of patients would be more likely to decline AIT if offered SCIT by their allergist, with 90% likely to pursue treatment if offered SLIT-tablets.⁴⁹

In the current study, as nearly 1 in 5 AIT patients discontinued treatment after the first visit, with nearly 25% never even receiving a single injection, taken together, results suggest that additional work and planning at the onset of treatment in the form of shared decision making may be needed to minimize health care waste and optimize therapeutic interventions for these patients. With the onset and continued presence of the COVID-19 pandemic in the United States, the American Academy of Allergy, Asthma, and Immunology has advised providers to modify AIT treatment schedules, which will contribute to SCIT discontinuation rates,⁵⁰ and further emphasizes the need for an ongoing dialogue between patients and their caregivers, potentially through shared decision making tools. However, this shift toward telemedicine may also present an

Table 4 All-cause health care utilization by AIT cohorts in the follow-up period

	≥25 AIT Fills (n = 45,279)	Any AIT Fills (n = 103,207)	No AIT Fills (n = 2,231,323)
Inpatient			
Patients with an inpatient hospitalization, n (%)	1091 (2.4)	3907 (3.8)	93,939 (4.2)
No. inpatient admissions, mean ± SD	0.0 ± 0.2	0.1 ± 0.3	0.1 ± 0.3
Length of stay, mean ± SD	3.2 ± 3.5	3.6 ± 5.1	3.6 ± 5.2
Outpatient services			
ED visits			
Patients with an ED visit, n (%)	8749 (19.3)	23,711 (23.0)	489,130 (21.9)
No. ED visits, mean ± SD	0.3 ± 0.7	0.4 ± 1.0	0.4 ± 1.0
Physician office visits			
Patients with a physician office visit, n (%)	44,862 (99.1)	100,874 (97.7)	2,222,327 (99.6)
No. physician office visits, mean ± SD	8.9 ± 7.9	8.5 ± 7.7	6.6 ± 5.5
Specialist office visits*			
Patients with a specialist office visit, n (%)	34,690 (76.6)	60,535 (58.7)	587,269 (26.3)
No. specialist office visits, mean ± SD	2.3 ± 3.8	1.7 ± 3.2	0.5 ± 1.2
Laboratory tests			
Patients with laboratory tests, n (%)	36,018 (79.5)	82,990 (80.4)	1,774,223 (79.5)
No. laboratory tests, mean ± SD	9.3 ± 13.9	11.1 ± 19.4	9.4 ± 17.0
Other outpatient services			
Patients with other outpatient services, n (%)	45,279 (100.0)	103,152 (99.9)	2,035,138 (91.2)
No. other outpatient services, mean ± SD	50.7 ± 14.9	31.7 ± 22.8	7.2 ± 11.4
Outpatient prescriptions			
Patients with an outpatient prescription, n (%)	43,386 (95.8)	97,854 (94.8)	2,060,781 (92.4)
No. outpatient prescriptions, mean ± SD	20.3 ± 21.1	20.5 ± 22.0	15.1 ± 18.8
Surgical procedures#			
Patients with a surgical procedure, n (%)	1909 (4.2)	4195 (4.1)	49,142 (2.2)
No. surgical procedures, mean ± SD	0.1 ± 0.5	0.1 ± 0.5	0.0 ± 0.3
Anaphylaxis reactions			
Patients with an anaphylaxis reaction, n (%)	993 (2.2)	1513 (1.5)	0 (0.0)
No. anaphylaxis reactions, mean ± SD	0.1 ± 0.8	0.1 ± 0.6	0.0 ± 0.0

AIT = Allergy immunotherapy; SD = standard deviation; ED = emergency department.

*Include allergy, immunology, otolaryngology, or pulmonary disease providers.

#Include turbinatectomy, endoscopic sinus surgery, septoplasty, tympanostomy, and nasal polypectomy.

opportunity for greater access to patients who may otherwise avoid in-office visits due to inconvenience or social distancing practices.

Limitations

Studying a disease such as AR in administrative claims provides some challenges. AR can often be managed without intervention of a health care professional, thus not producing any medical or pharmacy claims; therefore, the true length of disease for patients in the current sample is unknown. Additionally, the current study required a minimum of 2 years of continuous commercial health coverage. Consequently, results may not be generalizable to underserved AR patients with other types of insurance, including Medicaid beneficiaries where outcomes will likely differ,⁵¹ and to those without insurance. Also, though patients were followed up for 2 years, the

long-term clinical outcomes of AR will likely require an extended follow-up window as AIT therapy should persist for years. Also, administrative claims data are subject to data coding limitations and data entry error, which may result in missing or erroneous data. Finally, patients receiving SLIT-tablet prescriptions were also included in the analyses and may differ in some ways from those receiving SCIT. Analyses focused solely on SLIT-tablet patients may be warranted as a follow-up to the current investigation.

CONCLUSION

In summary, this study presents a real-world examination of AR in the United States. AIT remains the only available AR treatment that can induce allergen-specific immune tolerance, though continues to be

Table 5 AR-related health care utilization by AIT cohorts in the follow-up period*

	≥25 AIT Fills (n = 45,279)	Any AIT Fills (n = 103,207)	No AIT Fills (n = 2,231,323)
Inpatient			
Patients with an inpatient hospitalization, n (%)	76 (0.2)	294 (0.3)	4815 (0.2)
No. inpatient admissions, mean ± SD	0.0 ± 0.0	0.0 ± 0.1	0.0 ± 0.1
Length of stay, mean ± SD, days	2.4 ± 1.4	2.9 ± 2.2	2.8 ± .8
Outpatient services			
ED visits			
Patients with an ED visit, n (%)	3658 (8.1)	9959 (9.6)	208,549 (9.3)
No. ED visits, mean ± SD	0.1 ± 0.4	0.1 ± 0.5	0.1 ± 0.5
Physician office visits			
Patients with an physician office visit, n (%)	42,522 (93.9)	89,800 (87.0)	2,189,797 (98.1)
No. physician office visits, mean ± SD	4.5 ± 5.4	3.8 ± 4.7	2.8 ± 2.4
Specialist office visits#			
Patients with specialist office visit, n (%)	34,059 (75.2)	58,312 (56.5)	528,254 (23.7)
No. specialist office visits, mean ± SD	2.2 ± 3.7	1.6 ± 3.1	0.5 ± 1.1
Laboratory tests			
Patients with laboratory tests, n (%)	696 (1.5)	1762 (1.7)	33,600 (1.5)
No. laboratory tests, mean ± SD	0.0 ± 0.2	0.0 ± 0.2	0.0 ± 0.2
Other outpatient services			
Patients with other outpatient services, n (%)	45,279 (100.0)	102,897 (99.7)	1,253,091 (56.2)
No. other outpatient services, mean ± SD	44.8 ± 11.1	24.9 ± 20.2	1.4 ± 2.7
Outpatient prescriptions			
Patients with an outpatient prescription, n (%)	37,648 (83.1)	80,139 (77.6)	1,415,258 (63.4)
No. outpatient prescriptions, mean ± SD	6.3 ± 7.2	5.2 ± 6.8	2.6 ± 4.2
Surgical procedures§			
Patients with a surgical procedure, n (%)	1909 (4.2)	4195 (4.1)	49,142 (2.2)
No. surgical procedures, mean ± SD	0.1 ± 0.5	0.1 ± 0.5	0.0 ± 0.3
Anaphylaxis reactions			
Patients with an anaphylaxis reaction, n (%)	993 (2.2)	1513 (1.5)	0 (0.0)
No. anaphylaxis reactions, mean ± SD	0.1 ± 0.8	0.1 ± 0.6	0.0 ± 0.0

AR = Allergic rhinitis; AIT = allergy immunotherapy; SD = standard deviation; ED = emergency department; URTI = Upper respiratory tract infection

*AR-related values include all inpatient medical claims with a diagnosis code in the primary position or any position on outpatient claims for AR and AR-related diagnoses, including asthma, conjunctivitis, URTI, atopic dermatitis, etc., AR-related surgical procedures, anaphylaxis, and all pharmacy claims for an indicated for AR or AR-related treatment.

#Include allergy, immunology, otolaryngology, or pulmonary disease providers.

§Include turbinectomy, endoscopic sinus surgery, septoplasty, tympanostomy, and nasal polypectomy.

underutilized as a therapeutic option, with < 5% of AR patients in the current analysis having received this treatment, and less than half of these patients reaching the maintenance phase. It is likely that some proportion of patients were never offered this treatment. Results highlight the need for improved patient-treatment matching efforts to increase the AIT prescription and adherence rate among the AR population. Shared decision making will be critical for complete patient understanding of this complex treatment regimen, which may aid in identifying patients who may be candidates for SLIT-tablets (e.g., access issues for physician office

visits, phobias of shots) or other modes of therapy altogether.

However, despite low utilization, patients with the greatest need for AIT, as evidenced by higher allergy-related comorbidities, were more likely to initiate treatment in the current study. Results may suggest that AR patients are delaying the initiation of AIT until disease severity is critical. Regardless, among AIT patients reaching the maintenance phase, results from analyses spanning pre- to post-AIT initiation revealed notable reductions in all AR-related comorbidities assessed, along with reduced inpatient hospital and ER visits compared with both the

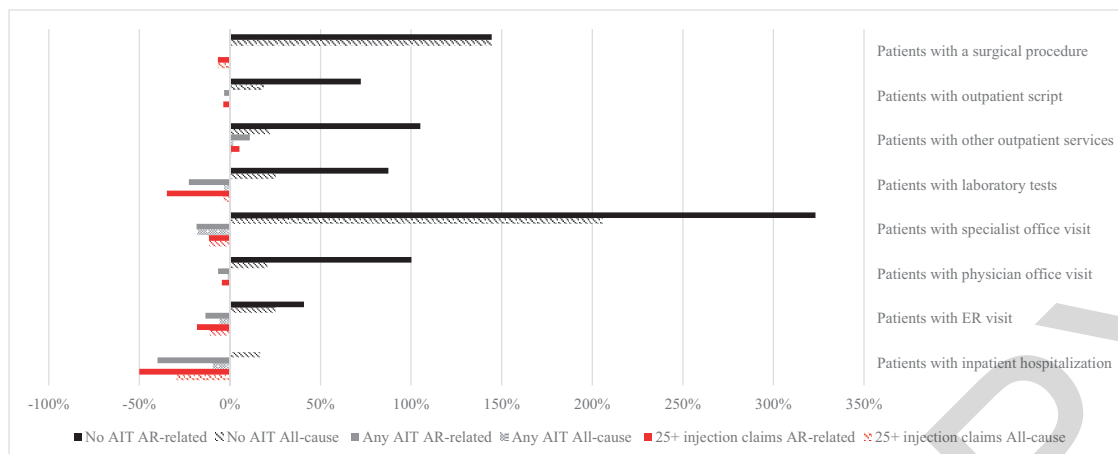


Figure 2. Change in all cause and allergic rhinitis (AR) related health care utilization from pre- to postperiod.

AIT cohort as a whole, and non-AIT patients. Continued efforts to increase patient awareness of available options and adherence to AIT, potentially through shared decision making and the use of digital technology, which has already shown effectiveness in promoting adherence,⁴⁸ will be essential to future patient treatment matching efforts, where the timing and proportion of AR patients identified for candidates for AIT is maximized.

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