Journal of Asthma and Allergy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Persistence and Reasons for Discontinuation of Subcutaneous Immunotherapy in Children with Dust Mite Allergy: A Real-World Cohort from Hangzhou, China

Zhenghong Song[1,*], Jing He[2,*], Shuxian Li[2], Kaiyi Lu[3], Hanqing Shao[1,2], Jinling Liu[2], Lei Wu[2], Hongzhen Xu[1], Zhimin Chen[2]

[1]Nursing Department, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, China; [2]Department of Pulmonology, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, China; [3]Hangzhou Normal University Department of Medical Administration, Hangzhou, China

*These authors have contributed equally to this work

Correspondence: Zhimin Chen, Department of Pulmonology, Children's Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, 310052, People's Republic of China, Email zmchen@zju.edu.cn; Hongzhen Xu, Nursing Department, Children's Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, 310052, People's Republic of China, Email 6184020@zju.edu.cn

Objective: To investigate the present state of adherence to subcutaneous specific immunotherapy (SCIT) in children sensitized to dust mites, explore the factors contributing to the cessation of SCIT in this demographic, and provide scientific evidence aimed at improving compliance and efficacy of SCIT in pediatric patients.

Methods: A retrospective analysis was conducted on clinical data of pediatric patients who received treatment at our desensitization center between January 2017 and December 2023. These children exhibited sensitivity to dust mites and were diagnosed with allergic asthma, allergic rhinitis, or other allergic diseases, subsequently undergoing SCIT therapy. The fulfillment of the SCIT regimen was evaluated, and the factors contributing to treatment cessation were analyzed.

Results: A total of 680 children were included in the study. Of these, 424 children (62.35%) successfully completed the entire treatment regimen (total course ≥3 years), whereas 256 children (37.65%) chose to discontinue the treatment prematurely (total course <3 years). The reasons for the cessation of SCIT, ranked from most to least common, included efficacy issues (54.69%), drug intolerance (18.75%), family-related factors (10.94%), the repercussions of the COVID-19 pandemic (6.64%), influence from other diseases (6.25%) and various other reasons. The primary reason for discontinuation within the first month was family factors (46.15%), while within six months, it was drug intolerance (40.82%), and after 6 months, efficacy issues (68.04%) became the leading cause.

Conclusion: The uncertain efficacy and intolerance to the medication predominantly hinder compliance with SCIT in children, while family factors serve as the main reason for discontinuation within the first month. By enhancing parental comprehension and awareness of SCIT, standardizing operational protocols, and promptly addressing any adverse reactions, compliance with SCIT could be significantly improved.

Keywords: children, house dust mite, specific immunotherapy, compliance

Introduction

Allergic asthma (AA) and allergic rhinitis (AR) rank as the most prevalent chronic airway allergic diseases in children, with an increasing incidence that significantly affects pediatric health and imposes considerable financial burdens on families and society.[1,2] The house dust mite (HDM) stands out as the primary allergen responsible for triggering respiratory allergies[3] Indeed, complete avoidance of allergens, particularly HDM, proves to be an elusive goal. While traditional pharmacological treatments, such as inhaled corticosteroid, continue to be the most commonly prescribed

https://doi.org/10.2147/JAA.S558029
Received: 19 August 2025
Accepted: 24 April 2026
Published: 4 May 2026

therapies for respiratory allergies, the long-term reliance on medication, alongside potential adverse effects and economic implications, should be carefully considered. Moreover, pharmacological interventions often address only the symptoms, with many patients experiencing a relapse upon cessation of treatment.

Allergen immunotherapy (AIT) is the sole treatment endorsed by the World Health Organization capable of altering the natural progression of allergic diseases, providing immune tolerance for many years even after the therapy concludes.[4–6] Currently, AIT is primarily administered through two routes: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT).[7] SCIT is the most prevalent and effective AIT modality in clinical practice, requiring repeated administration of allergen extracts over a duration of 3–5 years to establish immune tolerance.[7,8] The success of SCIT relies on the regularity allergen extract administration; therefore, adherence to SCIT is crucial for achieving satisfactory long-term outcomes. Previous studies showed that fewer than 20% of AIT patients persist with the treatment during the second year of 3 to 5-year therapeutic regimen.[9,10] In central China, Yang et al[11] reported 64.6% of SCIT patients completed 3 years of treatment. Besides, Lee et al[12] reported 19.6% of AIT patients failed to completed 3 years of treatment in Korea. The adherence rates of AIT vary largely across different regions.

This situation may lead to ineffective treatment, a waste of medical resources, and increased healthcare expenses. The World Health Organizaon posits that increased adherence could significantly influence the overall health of the population, more so than advancements in specific pharmaceutical therapies.[13] Hence, there is an urgent need to comprehend the reasons behind discontinuation at different stages of SCIT in order to bolster adherence and efficacy. The major factors associated with non-compliance include long duration of AIT, the frequency of injections, perceived efficacy, allergic reactions during vaccinations, and travel considerations; these factors are influenced by regional differences, health system structures, and cultural contexts.[14,15] While various factors influencing SCIT discontinuation are known, there is a lack of studies systematically analyzing how the relative importance or prevalence of these factors may vary at different stages (time points) during the treatment course. Most studies regarding SCIT compliance focuses on adult populations or general populations (comprising both adults and children); there is a scarcity of robust studies specially targeting children, both in sample size and duration.[16,17] Additionally, compare with the wide application of SCIT in AR and/or AA, it is currently unclear whether AIT is an effective treatment for patients with AD. Although several studies demonstrated positive effects of AIT in patients with AD, only a few data sets are available, thereby making reference value less robust.[18,19]

The digital transformation of healthcare sector, including mHealth and Artificial Intelligence, places the patient at the center of the healthcare system and revolutionizes the practice of medicine, especially in AIT.[20,21] The European Academy of Allergy and Clinical Immunology (EAACI) recommends that technology-driven patient-centered care can greatly improve clinical practice, particularly in the adherence and efficacy of AIT.[22] In this study, we utilized an integrated mobile and web-based platform called e-LinkCare (e-LinkCare, UBREATH®, Hangzhou, China) to facilitate the comprehensive management of the AIT course. This mobile technology integrates tools for overseeing AIT protocols, including patient information, injection records, and automated administrative tasks.

Hence, this study aimed to explore the reasons for discontinuation of AIT within a large pediatric cohort from January 2017 to December 2023 in Hangzhou, China, thereby providing scientific evidence for effective strategies to improve treatment adherence in children undergoing SCIT.

Materials and Methods

Study Population

Pediatric patients diagnosed with HDM-sensitized AR, AA, or atopic dermatitis (AD) who underwent SCIT at the Allergy Clinic of the Respiratory Department, Children's Hospital, Zhejiang University School of Medicine, from January 2017 to December 2023, were included in this study. Patients who transferred care or were still undergoing SCIT at the time of analysis due to uncertainty regarding their completion of the full treatment course were excluded. To enhance the reliability of our findings on reasons for SCIT discontinuation, we focused specifically on patients who had already concluded their SCIT regimen—whether they completed the full course or not (Figure 1).

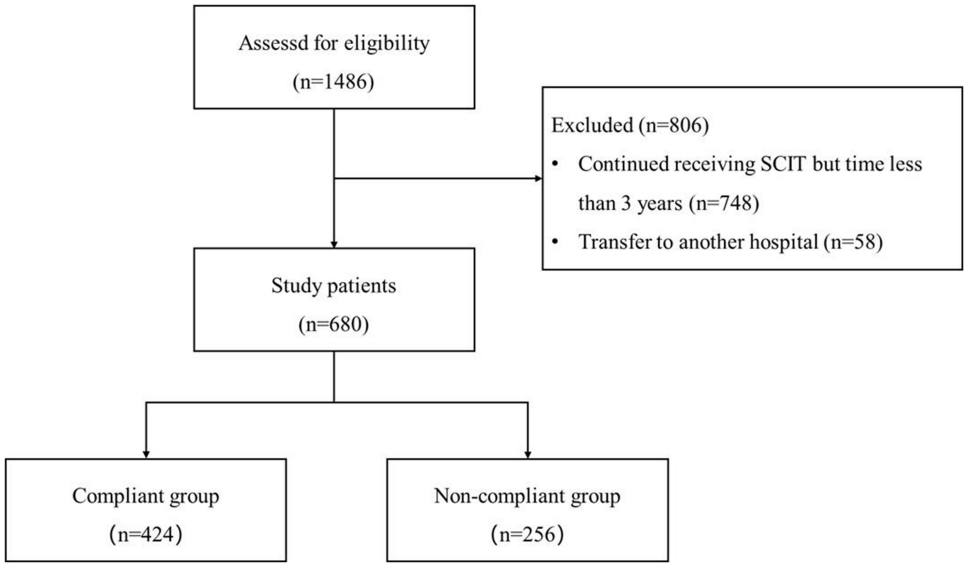

Figure 1 Flow chart for patient selection.

SCIT was administered to patients with AR and/or AA sensitized to HDM who exhibited uncontrolled respiratory allergic symptoms, in conjunction with medical therapy and the implementation of avoidance strategies. This treatment was targeted towards individuals with moderate to severe AR and mild to moderate AA, while those with mild AR and severe AA were excluded. In detail, moderate-to-severe AR was defined according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines,[23] referring to patients with symptoms that are bothersome and affect daily activities or sleep. Mild-to-moderate AA was defined based on the Global Initiative for Asthma (GINA) criteria,[24] covering patients with well-controlled or partially controlled asthma on low-to-medium dose inhaled corticosteroids. Given the use of SCIT for AD remains controversial, we provide SCIT to HDM-sensitized children with AD, following the acquisition of written consent from their guardians.

This study was conducted in accordance with the Declaration of Helsinki and approved by ethics committee of Children's Hospital, Zhejiang University School of Medicine (Ethics Approval No.: 2022-IRB-216). Written informed consent was obtained from the guardians of all subjects prior to SCIT treatment and the study.

Diagnosing HDM Sensitized AR, AA, and AD

The diagnoses and conventional medical therapies for AR, AA and AD were based on ARIA,[23] GINA[24] and the expert consensus statement on the diagnosis and treatment of AD in children in China (2017),[25] respectively. Prior to the initiation of SCIT, all patients underwent serum allergen testing that showed elevated serum immunoglobulin E (sIgE) levels specific to HDM. This was characterized by serum concentrations of Der p- and/or Der f-sIgE $\geq$ 0.35 kUA/L, considered a positive result, including mono-HDM sensitized and mixed sensitized conditions. Mono-HDM sensitization was defined as being positive only for HDM, with sIgE levels to other inhalant allergens below 0.35 kUA/L. Mixed sensitization was defined as an elevated HDM sIgE level predominating alongside positive sensitivity to other inhalant allergens (serum sIgE $\geq$ 0.35 kUA/L). Additionally, skin prick test revealed positive responses of moderate or greater intensity to HDM ($\geq$ ++), confirming sensitization to HDM.

Administration of SCIT and Digital Management System

The standardized HDM-specific SCIT was performed at the allergic clinic of respiratory department. The patients received subcutaneous injections of the aluminum-formulated Der p Alutard SQ vaccine (ALK-Abello A/S, Horsholm, Denmark). The treatment protocol followed the recommended up-dosing schedule over a span of 16 weeks, culminating

https://doi.org/10.2147/JAA.S558029

in the peak maintenance dose of 100,000 Alutard SQ. Subsequently, this maximum maintenance dose was administered every 6 weeks for a duration of 3–5 years.[20] Following each administration, patients were monitored in the outpatient setting for a minimum of thirty minutes to observe and mange any immediate adverse reactions. The grade of systemic adverse reaction of SCIT refers to the WAO grading standard (2020),[26] with a higher grade indicating greater severity. Grade 1 is defined as isolated symptoms affecting a single organ system (eg, skin, upper respiratory tract, conjunctiva). Grade 2 is characterized by multi-organ involvement, including mild asthma (responsive to bronchodilators), gastro-intestinal symptoms, or uterine cramps. Grade 3 is characterized by severe, unresponsive lower respiratory impairment or upper airway edema (larynx, uvula, tongue). Grade 4 denotes life-threatening conditions such as respiratory failure or hypotension (with/without loss of consciousness). Grade 5 represents the fatal outcome of SCIT-related systemic adverse reactions.

A digital management system designed by e-LinkCare. UBREATH® (Zhejiang Hangzhou, China) was utilized for the precise and efficient oversight of SCIT patients in the study. An extensive array of information was documented within this system, including patient demographics (eg. age, gender, allergic diseases, allergens. etc.), contact information of guardians, enrollment dates, treatment records (including the number of injections, dosages, times of injection, sites of injection, adverse reactions and subsequent treatments), and completion or dropout date.

One the one hand, this app system can automatically send injection reminders to guardians of patients who fail to receive treatment on time throughout the course of treatment. On the other hand, patients who did not adhere to the recommended scheduled for injections were also monitored weekly by specialized nurses, who reached out to their guardians to ascertain the reasons for any missed appointments and to document these incidents. Therefore, the treatment records were accurate and reliable, and the variables included in this study were complete.

Compliance Assessment Criteria

Treatment adherence was characterized as the receipt of SCIT following the designated treatment regimen for a minimum duration of three years.[20] In present study, a three-month interruption is commonly used to define significant treatment discontinuation in long-term injection, which aligns with previous study.[11,17] Furthermore, in clinical practice, delaying injections beyond this timeframe can substantially compromise dosing efficacy, necessitate dose re-titration, require additional hospital visits for dose adjustment, or even involve re-initiation of the treatment regimen. Therefore, patients experiencing a delay of three consecutive months from their advised treatment schedule and/or whose guardians opted to terminate the treatment within the three-year SCIT period were categorized as having drop-out, with the reasons for discontinuation duly documented.[21] In this study, children who finished at least 3 years of uninterrupted treatment were classified within the compliant group, while those who ceased treatment prior to the three-year mark were assigned to the drop-out group.

Statistical Analysis

All statistical analysis were conducted utilizing SPSS software (version 26.0). All data variables included in this study were fully recorded with no missing values. Continuous variables of normal distribution (Kolmogorov–Smirnov test) were expressed as mean and standard deviation, whereas those with non-normal distribution were depicted by median (M) and interquartile range (IQR). The evaluation of continuous variables was conducted using 2-sample t tests, while the Mann-Whitney U tests were employed to compare nonparametric variables. To ascertain the association between categorical variables, the Pearson chi-square test and Fisher's exact test were used. Bonferroni method was used for multiple comparison correction. A two-tailed α of 0.05 was established for all tests, with $p < 0.05$ deemed statistically significant.

Results

Baseline Information and Compliance of SCIT (January 2017 and December 2023)

Between January 2017 and December 2023, a total of 1486 pediatric patients underwent HDM-specific SCIT at our hospital's respiratory center. Of these patients, 680 completed the treatment (including those who drop-out), while 806 children continued their SCIT throughout the study duration. Among those who concluded the therapy, 256 ceased SCIT prior to the recommended minimum of three years, whereas 424 successfully completed the SCIT regimen lasting three to five years. The overall compliance rate of SCIT was 62.35% (424/680).

Excluding the children who were still receiving treatment during the study period and those transferred to another hospital for SCIT, a total of 680 children were selected for further analysis, divided into compliant group (n=424) and drop-out group (n=256) based on the aforementioned definitions. No statistically significant differences were observed between the two groups in terms of gender, age at the onset of SCIT, and place of residence ($P > 0.05$). The duration of treatment in the drop-out group was significant shorter than that of compliant group (1305.5 days vs. 469.0 days, $p < 0.001$). A summary of the demographic characteristics of the patients was listed in Table 1.

In the cohort of individuals who discontinued treatment, 13 patients (5.08%) ceased SCIT in less than 1 month, 18 patients (7.03%) withdrew within 3 months, 31 patients (12.11%) terminated treatment between the third to sixth month, 46 patients (17.97%) discontinued from the sixth to twelfth month, 87 patients (33.98%) exited from the twelfth to twenty-fourth month, and 61 patients (23.83%) ceased treatment from thetwenty-fourth to the thirty-sixth month.

Efficacy Concerns and Intolerance of SCIT Mainly Affected Compliance

In our study, the factors influencing adherence to SCIT, ranked from highest to lowest, included efficacy concerns (54.69%), intolerance to SCIT (18.75%), family influences (10.94%), the repercussions of COVID-19 (6.64%), other health conditions (6.25%), a transition to traditional Chinese medicine (1.17%), and inability to establish contact (1.56%) (Table 2).

For discontinuation stemming from efficacy concerns, 126 children withdrew due to ambiguous treatment outcomes (the ineffectiveness or minimal impact of SCIT acknowledge by their guardians and medical professionals), with an average treatment duration of 17.9 months. Interestingly, the remaining 14 children ceased SCIT treatment simple because their guardians perceived the improvements to be substantial enough to render further treatment unnecessary; this occurred during the maintenance phase of SCIT, with an average treatment duration of

Table 1 Children Characteristics of SCIT Treatment

Characteristics	Compliant Group (n=424)	Non-Compliant Group (n=256)		*P value*
Gender, n (%)			0.072[a]	0.789
Male	294 (69.3%)	175 (68.4%)		
Female	130 (30.7%)	81 (31.6%)		
SCIT start age (years)	7.0 (6.0–9.0)	7.0 (6.0–9.0)	0.667[b]	0.505
SCIT start age categories				
5–8 years, n (%)	289 (68.2%)	171 (66.8%)	0.934[a]	0.627
9–12 years, n (%)	124 (29.2%)	75 (29.3%)		
>12 years, n (%)	11 (2.6%)	10 (3.9%)		
Living areas, n (%)			5.760[a]	0.098
Hangzhou Area	361 (85.1%)	200 (78.1%)		
Surrounding Areas of Hangzhou	27 (6.4%)	24 (9.4%)		
Other Areas in Province	35 (8.3%)	31 (12.1%)		
Out of Province	1 (0.2%)	1 (0.4%)		
Treatment duration (days), median (IQR)	1305.5 (1204–1421)	469.0 (197.8–704)	−21.782[b]	<0.001*
Injection numbers, median (IQR)	45 (41–46)	25 (18–30)	−21.872[b]	<0.001*

Notes: [a]Chi-square test, [b]Mann-Whitney test, *$P < 0.05$.
Abbreviations: IQR, 25% to 75% interquartile range.

https://doi.org/10.2147/JAA.S558029

Table 2 Distribution of Reasons for Discontinuation of SCIT in Children

Discontinuation Reasons	Patients	Percentage (%)
Efficacy Issues	140	54.7
SCIT intolerance	48	18.7
Family Factors	28	11.0
COVID-19 impact	17	6.6
Other diseases	16	6.2
Switch to Chinese traditional medicine	3	1.2
Cannot contact	4	1.6

20.5 months. Among the 48 children who discontinued treatment due to intolerance, 30 patients encountered adverse reactions (AEs) related to SCIT, with immediate systemic reactions occurring within half an hour after injection (24 cases) being the most prevalent. In total systemic reactions, Grade 1 was recorded 80 times, Grade 2 occurred 6 times and Grade 3 was noted 4 times, all of which were relieved immediately following symptomatic treatment. Thirteen patients experienced systemic reactions more than three times. Despite adjustments made to reduce the injection dosage and/or splitting it into two separate injections, they remained intolerant and withdrew from treatment. Four children who exhibited moderate to severe systemic reactions were administered epinephrine injections and recovered without severe repercussions; however, their parents opted to discontinue treatment due to perceived future risks. Additional AEs included delayed systemic reactions (4 cases of asthma attacks occurred beyond 30 minutes) and local AEs at the injection site (2 cases of injection site swelling exceeding 5 cm in diameter). Furthermore, 18 children terminated treatment due to exacerbated dermatitis symptoms (including dermatitis that emerged during the course of treatment).

In this study, grade 1 systemic reactions were frequently observed and had a minimal effect on compliance with SCIT. Nevertheless, the intensity of adverse reactions exhibited a notable correlation with treatment discontinuation, demonstrating a statistically significant difference ($P < 0.05$), as illustrated in Table 3.

Among the factors contributing to dropout rates, 13 cases were attributed to pediatric reasons, with 9 children relocation for educational purposes and 4 opting to discontinue treatment due to psychological issues during adolescence. Parent-related factors accounted for 15 cases. Of these, 5 parents deemed the lack of time for transportation and the prolonged treatment duration as inconvenient. Meanwhile, 2 parents perceived their child's symptoms as "mild", deeming SCIT unnecessary, while 8 parents expressed significant concerns regarding SCIT. For the latter group, 5 cases ceased treatment after just one injection due to disagreements among family members. The influence of the COVID-19 pandemic and comorbidity on SCIT adherence was minimal, with only 17 patients interrupting their treatment due to fears of contracting COVID-19, and 8 children maintaining treatment regimens that lasted nearly 3 years. Additionally, 16 children halted their treatment due to the emergence of other diseases during SCIT, including contraindications for the therapy.

Table 3 Impact of Systemic Adverse Reactions on SCIT Compliance

Systemic Adverse Reaction	Compliant (n=424)	Non-Compliant (n=256)		*P value*
Occurrence patients	149 (35.1)	75 (29.3)	2.468[a]	0.116
Occurrence injections	770 (4.2)	274 (4.6)	0.736[a]	0.391
Grade of injections				0.043[c,*]
Grade 1	752 (97.7)	264 (96.3)		
Grade 2	17 (2.2)	6 (2.2)		
Grade 3	1 (0.1)	4 (1.5)		

Notes: [a]Chi-square test, [c]Fisher's exact test, *$P < 0.05$, Systemic adverse reaction grade refers to the WAO grading standard, with a higher grade indicates greater severity.

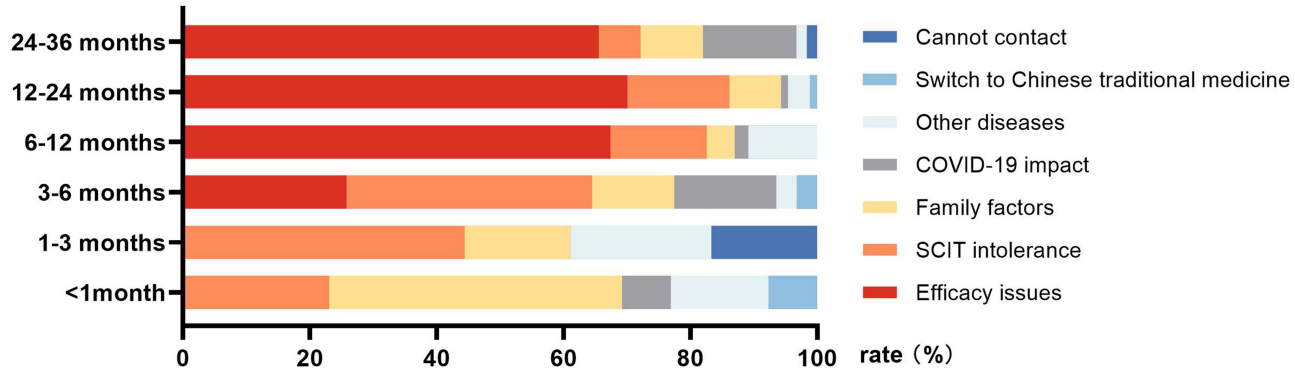

Figure 2 The reasons for SCIT dropout in children varied at different discontinuation times.

Main Factors for Discontinuing SCIT Varied at Different Cessation Times

In the group of individuals who discontinued treatment, 60 children (23.44%) ceased their therapy during the initiation phase of SCIT and, while 196 children (76.56%) did so in the maintenance phase. Furthermore, 108 patients (42.19%) terminated their treatment in the first year, 87 cases (33.98%) in the second year, and 61 cases (23.83%) during the third year, with the proportion gradually decreasing each subsequent year.

By examining the patterns of drop-out occurrences, we discovered that the predominant factors influencing dropout varied according to different termination periods. Within the initial month, family-related issue (46.15%) emerged as the most prevalent reason, whereas intolerance to SCIT (38.71–44.44%) became the principal cause for discontinuation of therapy during the first to sixth month. For those exceeding six months, concerns regarding efficacy (65.6–70.11%) surfaced as the primary factor impacting adherence to SCIT, followed by treatment intolerance (15.22–16.10%) (Figure 2).

Impact of Reasons for SCIT on Treatment Adherence in Children

Among the 680 children who successfully completed the SCIT course, the predominant reason for undergoing SCIT was a combination of AR and AA (n=329, 48.38%), followed by AR (n=305, 44.85%), AA (n=36, 5.29%), and AD (n=10, 1.47%). Notably, all children solely diagnosed with AD who underwent SCIT experienced interruptions in their treatment, which led to a complete exacerbation of dermatitis symptoms (100%).

The rates of adherence and dropout exhibited considerable variation regarding the reasons for SCIT ($p<0.001$) (Table 4). A more in-depth analysis indicated the dropout rate within the AD group was significant elevated in comparison to the other three groups (100%, $p < 0.001$ for all, as determined by Fisher's exact test). Furthermore, a statistical difference in dropout rates was noted between the AR group and the AA group (43.93% vs. 19.44%, $p = 0.005$), as well as between the AR group and the AA+AR group (43.93% vs. 31.91%, $p = 0.002$). Conversely, there was no notable difference on the dropout rates between the AA group and AA+AR group (19.44% vs. 31.91%, $p > 0.05$).

Table 4 The Impact of the Reason for SCIT on Treatment Compliance

The Reason for SCIT	Total	Compliant	Non-Compliant	*P* value	Adjusted *P* Value (Bonferroni Correction)			
					AA	AR	AA+AR	AD
AA	36 (5.3)	29 (80.6)	7 (19.4)	<0.001[c,*]	-	0.004	0.133	<0.001
AR	305 (44.9)	171 (56.1)	134 (43.9)		0.004	-	0.002	<0.001
AA+AR	329 (48.3)	224 (68.1)	105 (31.9)		0.133	0.002	-	<0.001
AD	10 (1.5)	0 (0)	10 (100)		<0.001	<0.001	<0.001	-

Notes: [c]Fisher's exact test, *$P < 0.05$, Bonferroni correction adjusted $\alpha = 0.05/6 = 0.0083$, AD for SCIT was a exploratory treatment.
Abbreviations: AA, allergic asthma; AR, allergic rhinitis; AA+AR, allergic asthma and allergic rhinitis; AD, atopic dermatitis.

https://doi.org/10.2147/JAA.S558029

Discussion

Compliance plays a vital role in maximizing the effectiveness of SCIT, and identifying these determinants can greatly improve treatment outcomes. Recent studies on SCIT adherence have yield varied findings, influenced by factors such as geographical location, study methodology, and demographic characteristics. Previous studies examining adherence to SCIT showed mixed results with adherence rates ranging from 23 to 89%.[27,28] Between January 2017 and December 2023, our hospital's respiratory center administered SCIT to 1486 pediatric patients, with 256 discontinuing treatment and 424 completing the course, resulting in a compliance rate of 62.35% (424/680), which is comparable to domestic report[11] and higher than most similar studies conducted internationally.[29] This moderate compliance rate may be attribute to the fact that all participants in this research were children, in line with other studies, indicating that SCIT compliance among children is generally superior to that of adults.[30,31] Some studies have shown that younger patients often experience improved therapeutic outcomes from SCIT.[32,33] Moreover, parents, as pivotal influence in pediatric care, frequently exhibit a robust desire and commitment to support their child's treatment, which may enhance treatment adherence. Additionally, a significant portion of our center's patients consisted of younger children, and the early adoption of digital precision management for allergic diseases likely fostered the increased compliance rates.[34]

In this study, a digital management app was applied in the whole course of SCIT treatment, in which the basic information and treatment records of the patient were recorded in detail and dynamically. Importantly, doctors can identify which patients have not adhered to their scheduled treatment each week, and the digital system can automatically send treatment injection reminders to the guardians until the injection is administered. For patients and guardians, if they are unable to receive the scheduled injection due to unforeseen circumstances, they can submit a leave request and state the reason on the app. Simultaneously, specialized nurses would call the patient's guardian whose injections have been overdue for two weeks, using the contact information on the app, to remind them to complete the treatment on time. Facilitated by this application, automatic communication and enhanced engagementconnection between doctors and patients make it easier to monitor treatment and improve adherence.

Our findings in this study reveal that the foremost reasons of discontinuation of SCIT were issues related to efficacy and drug intolerance, in consistent with conclusions from previous studies.[11] The uncertainty expressed by parents regarding the effectiveness of the treatment emerged as the most important influence on pediatric SCIT adherence. Some parents perceived the initial treatment as effective during SCIT process, yet later observed a plateau in the therapeutic benefits, prompting them to unilaterally terminate the therapy when their expectations were not fulfilled. Furthermore, other parents prematurely ceased the administration of allergy medications, such as anti-histamines and inhaled glucocorticoids, leading to less optimal outcomes. In this study, 8 children halted treatment during the initial phase due to doubts surrounding SCIT efficacy, highlight the vital importance of health education prior to initiating SCIT. Therefore, it is essential to provide parents with realistic expectations regarding SCIT outcomes and emphasize the necessity of continuing symptomatic medication before embarking on SCIT. Additionally, a declining trend in drop-out rates was observed over the first, second, and third years of SCIT, which in consistent with clinical practice indicating that the benefits of SCIT become increasing evident as treatment progresses. Consequently, ensuring compliance during the first year is particularly crucial.

In contrast to uncertainties regarding efficacy, 14 children (5.47%) in this study discontinued SCIT prematurely because their parents believed the treatment had already achieved adequate effectiveness. When compared to other studies, the number and patients of patients terminating for this reason were relatively modest.[34] This might be attributed to our center's ongoing health education and communication with patients and their families throughout the treatment journey. Nevertheless, this reason for dropout still merits attention. For instance, two children with in our center concluded SCIT around the second year due to marked improvements, only to recommence treatment six months later when their allergy symptoms exacerbated. Such occurrences may result in a waste of medical resources and an increased financial burden on families and society. Therefore, healthcare providers must place significant emphasis on patient education and maintain close communication during treatment, underscoring the necessity of completing a treatment course lasting at least three years to secure sustained and long-term benefits.

The intensity of adverse reactions significantly influences patient adherence to SCIT. Our study found that drug intolerance, accounting for 18.75%, was the second most pivotal factor contributing to SCIT discontinuation. It is imperative for specialized practitioners and nursing staff to establish standardize SCIT treatment protocols while improving comprehensive patient management. Prior to each subcutaneous injection, a comprehensive evaluation of the child's condition should be undertaken to proactively address those at elevated risk for adverse reactions. For children with recurrent adverse reactions, prompt and suitable modifications to the treatment plan and dosage should be implemented, potentially in conjunction with the introduction of omalizumab.[35,36] Adherence to established protocols during injections, vigilant post-injection monitoring, and effective emergency response measures are essential to prevent severe adverse reactions.

Previous studies, have pinpointed a range of inconveniences as significant determinants affecting SCIT adherence.[11,37] Nonetheless, in our study, only 5 children ceased treatment for this reason. This phenomenon may be linked to the developed economy and accessible transportation in Zhejiang province, in addition to the abundant provision of SCIT in local healthcare facilities. Our center proactively offered referral services to assist patients encountering transportation obstacles. This measure also enabled many children to continue their treatment at nearby hospitals, thereby minimizing interruptions, especially during COVID-19 pandemic.

Our study also revealed that the rationale behind SCIT influence compliance rates. Children with asthma or with both a AA and AR exhibited higher adherence levels compared to peers suffering solely from AR, which was rarely documented in other studies.[11,15,38] Parents tend to underestimate the detrimental effects of AR, perceiving impact on growth, daily activities, and educational pursuits as less significant than that of asthma, or they believe that AR symptoms will as their children mature. Among those who halted SCIT due to uncertainties regarding its effectiveness, the majority were AR patients, comprising 81 cases (64.27%). Despite numerous national and international guidelines advocating for SCIT in the management of respiratory allergies instigated by dust mites,[8,39] not all individuals experience satisfactory efficacy. Furthermore, SCIT has been incorporated into guidelines for AD, although its effectiveness remains a subject of debate.[19,40] Our center has recently commenced investigation into SCIT for AD; however, the outcomes have not met expectation. In this study, 10 children who attempted to undergo SCIT for AD improvement discontinued the treatment midway due to worsening dermatitis following injections. Therefore, clinical decisions pertaining to SCIT for AD patients should be approached with caution. However, because the AD sample size was relatively small, this finding should be regarded as merely an exploratory result and necessitates validation in larger cohorts.

This study has some limitations. First, this single-center design may restrict the generalizability of the findings. Nevertheless, our study included a relatively large sample size and covered an extended timeframe. These features strengthen the internal validity of our results and provide valuable insights that can inform clinical practice and future research in similar settings. The assessment of perceived efficacy in this study relied primarily on reports from children and their parents, rather than on systematically collected symptom/medication scores or biomarker data such as HDM-sIgE and tIgE levels or lung function tests. This limits our ability to provide more definitive evidence of clinical efficacy. At the same time, in the context of this real-world study, parents and guardians in China typically observe their children closely on a daily basis and are highly attentive to changes in their health and well-being. Their concerns regarding treatment efficacy, though subjective, do reflect meaningful patient-centered outcomes and can offer valuable insights into real-world persistence and satisfaction with therapy. We plan to incorporate more objective efficacy measures in future studies to better capture and quantify treatment response. Furthermore, the retrospective design and limited clinical indicators did not permit multivariable adjustment for potential confounders. Therefore, the associations observed in univariate analyses should be interpreted as preliminary and warrant confirmation in larger, prospective studies designed for such modeling. As a single-center study conducted in an urban, relatively affluent pediatric population, our results may reflect local clinical protocols, socioeconomic factors, and patient demographics that limit generalizability. These contextual features underscore the need for caution when interpreting the univariate associations observed here. We also now explicitly position our work as an initial, hypothesis-generating step—one that highlights the importance of treatment adherence in pediatric SCIT but awaits validation in larger, multi-center cohorts with greater demographic and clinical diversity. Future prospective studies with larger cohorts are needed to validate these findings and to utilize robust multivariable models, such as logistic regression or Cox proportional hazards, to identify independent predictors

of SCIT adherence. Nonetheless, the study is grounded in a substantial real-world cohort of pediatric SCIT interventions, and the duration of the study is comparatively extensive, thereby yielding valuable insights into the improvement for SCIT adherence.

Conclusion

Our study demonstrated a moderate compliance rate of SCIT in the pediatric population, and the foremost reasons for discontinuation of SCIT were issues related to efficacy and drug intolerance. Furthermore, our study demonstrates distinct phases of dropout reasons, highlighting the need for stage-specific interventions to improve adherence, such as family counseling at the initiation phase, AE monitoring during dose escalation and expectation management in the maintenance phase. In an exploratory subgroup analysis, all pediatric patients with atopic dermatitis discontinued SCIT, suggesting that SCIT may not be suitable for this population. However, given the limited sample size and exploratory nature of this finding, further investigation is warranted to confirm these observations.

Acknowledgments

The authors are grateful of the doctors and nurses of desensitization clinic in the hospital for their help in data collection.

Author contributions

Zhenghong Song and Jing He contributed equally to this work and share first authorship. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the grant from Key R & D Program of Zhejiang Province (No.2024C03177) and the Zhejiang Province Medical and Health Science and Technology Plan (2024KY121).

Disclosure

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Vieira RJ, Sousa-Pinto B, Bousquet J, et al. Allergic rhinitis and its impact on asthma (ARIA)-EAACI guidelines-2024-2025 revision: Part II-guidelines on oral and ocular treatments. *Allergy*. 2026. doi:10.1111/all.70305
2. Venkatesan P. GINA report for asthma. *Lancet Respir Med*. 2025. doi:10.1016/s2213-2600(25)00242-5
3. Huang HJ, Sarzsinszky E, Vrtala S. House dust mite allergy: the importance of house dust mite allergens for diagnosis and immunotherapy. *Mol Immunol*. 2023;158:54–67. doi:10.1016/j.molimm.2023.04.008
4. Pfaar O, Bachert C, Bufe A, et al. Guideline on allergen-specific immunotherapy in IgE-mediated allergic diseases: S2k Guideline of the German Society for Allergology and Clinical Immunology (DGAKI), the Society for Pediatric Allergy and Environmental Medicine (GPA), the Medical Association of German Allergologists (AeDA), the Austrian Society for Allergy and Immunology (ÖGAI), the Swiss Society for Allergy and Immunology (SGAI), the German Society of Dermatology (DDG), the German Society of Oto- Rhino-Laryngology, Head and Neck Surgery (DGHNO-KHC), the German Society of Pediatrics and Adolescent Medicine (DGKJ), the Society for Pediatric Pneumology (GPP), the German Respiratory Society (DGP), the German Association of ENT Surgeons (BV-HNO), the Professional Federation of Paediatricians and Youth Doctors (BVKJ), the Federal Association of Pulmonologists (BDP) and the German Dermatologists Association (BVDD). *Allergo J Int*. 2014;23(8):282–319. doi:10.1007/s40629-014-0032-2
5. Kristiansen M, Dhami S, Netuveli G, et al. Allergen immunotherapy for the prevention of allergy: a systematic review and meta-analysis. *Pediatr Allergy Immunol*. 2017;28(1):18–29. doi:10.1111/pai.12661
6. Batard T, Taillé C, Guilleminault L, et al. Allergen immunotherapy for the prevention and treatment of asthma. *Clin Exp Allergy*. 2025;55 (2):111–141. doi:10.1111/cea.14575
7. Nakagome K, Nagata M. Allergen immunotherapy in asthma. *Allergol Int*. 2024;73(4):487–493. doi:10.1016/j.alit.2024.05.005
8. Alvaro-Lozano M, Akdis CA, Akdis M, et al. EAACI allergen immunotherapy user's guide. *Pediatr Allergy Immunol*. 2020;31 Suppl 25 (Suppl 25):1–101. doi:10.1111/pai.13189

9. Demoly P, Passalacqua G, Pfaar O, et al. Patient engagement and patient support programs in allergy immunotherapy: a call to action for improving long-term adherence. *Allergy Asthma Clin Immunol*. 2016;12:34. doi:10.1186/s13223-016-0140-2
10. Kiel MA, Röder E, Gerth van Wijk R, et al. Real-life compliance and persistence among users of subcutaneous and sublingual allergen immunotherapy. *J Allergy Clin Immunol*. 2013;132(2):353–60.e2. doi:10.1016/j.jaci.2013.03.013
11. Yang Y, Wang Y, Yang L, et al. Risk factors and strategies in nonadherence with subcutaneous immunotherapy: a real-life study. *Int Forum Allergy Rhinol*. 2018;8(11):1267–1273. doi:10.1002/alr.22190
12. Lee JH, Lee SH, Ban GY, et al. Factors associated with adherence to allergen specific subcutaneous immunotherapy. *Yonsei Med J*. 2019;60 (6):570–577. doi:10.3349/ymj.2019.60.6.570
13. Sabaté, Eduardo; World Health Organization. Noncommunicable diseases and mental health cluster. (2001). Adherence to long-term therapies: policy for action: meeting report, 4-5 June 2001. World Health Organization. Available from: https://iris.who.int/handle/10665/66984. Accessed April 28, 2026.
14. Gehrt F, Xu Q, Baiardini I, et al. Adherence in allergen immunotherapy: current situation and future implications. *Allergol Select*. 2022;6:276–284. doi:10.5414/alx02318e
15. Musa F, Al-Ahmad M, Arifhodzic N, et al. Compliance with allergen immunotherapy and factors affecting compliance among patients with respiratory allergies. *Hum Vaccin Immunother*. 2017;13(3):514–517. doi:10.1080/21645515.2016.1243632
16. Incorvaia C, Mauro M, Ridolo E, et al. Patient's compliance with allergen immunotherapy. *Patient Prefer Adherence*. 2008;2:247–251. doi:10.2147/ppa.s3806
17. Aytekin ES, Soyer Ö, Şekerel BE, et al. Subcutaneous allergen immunotherapy in children: real life compliance and effect of COVID-19 pandemic on compliance. *Int Arch Allergy Immunol*. 2021;182(7):631–636. doi:10.1159/000514587
18. Ridolo E, Martignago I, Riario-Sforza GG, et al. Allergen immunotherapy in atopic dermatitis. *Expert Rev Clin Immunol*. 2018;14(1):61–68. doi:10.1080/1744666x.2018.1401469
19. Yepes-Nuñez JJ, Guyatt GH, Gómez-Escobar LG, et al. Allergen immunotherapy for atopic dermatitis: systematic review and meta-analysis of benefits and harms. *J Allergy Clin Immunol*. 2023;151(1):147–158. doi:10.1016/j.jaci.2022.09.020
20. Bousquet J, Ansotegui IJ, Anto JM, et al. Mobile technology in allergic rhinitis: evolution in management or revolution in health and care? *J Allergy Clin Immunol Pract*. 2019;7(8):2511–2523. doi:10.1016/j.jaip.2019.07.044
21. Bousquet J, Hellings PW, Agache I, et al. Allergic rhinitis and its impact on asthma (ARIA) phase 4 (2018): change management in allergic rhinitis and asthma multimorbidity using mobile technology. *J Allergy Clin Immunol*. 2019;143(3):864–879. doi:10.1016/j.jaci.2018.08.049
22. Bousquet J, Shamji MH, Anto JM, et al. Patient-centered digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach - ARIA-EAACI Task Force Report. *Allergy*. 2023;78(7):1758–1776. doi:10.1111/all.15740
23. Brożek JL, Bousquet J, Agache I, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol*. 2017;140(4):950–958. doi:10.1016/j.jaci.2017.03.050
24. Reddel HK, Bateman ED, Becker A, et al. A summary of the new GINA strategy: a roadmap to asthma control. *Eur Respir J*. 2015;46(3):622–639. doi:10.1183/13993003.00853-2015
25. Pediatric Dermatology Group, Chinese Society of Dermatology. Diagnosis and treatment of atopic dermatitis in children in China: an expert consensus statement (2017). *Chin J Dermatol*. 2017;50(11):784–789. doi:10.3760/cma.j.issn.0412-4030.2017.11.002.
26. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J*. 2020;13(10):100472. doi:10.1016/j.waojou.2020.100472
27. Makatsori M, Senna G, Pitsios C, et al. Prospective adherence to specific immunotherapy in Europe (PASTE) survey protocol. *Clin Transl Allergy*. 2015;5:17. doi:10.1186/s13601-015-0060-0
28. Passalacqua G, Baiardini I, Senna G, et al. Adherence to pharmacological treatment and specific immunotherapy in allergic rhinitis. *Clin Exp Allergy*. 2013;43(1):22–28. doi:10.1111/j.1365-2222.2012.04052.x
29. Park MJ, Kapoor S, Yi J, et al. Systematic review of real-world persistence and adherence in subcutaneous allergen immunotherapy. *Int Forum Allergy Rhinol*. 2023;13(3):255–264. doi:10.1002/alr.23078
30. Liu W, Zeng Q, He C, et al. Compliance, efficacy, and safety of subcutaneous and sublingual immunotherapy in children with allergic rhinitis. *Pediatr Allergy Immunol*. 2021;32(1):86–91. doi:10.1111/pai.13332
31. Leader BA, Rotella M, Stillman L, et al. Immunotherapy compliance: comparison of subcutaneous versus sublingual immunotherapy. *Int Forum Allergy Rhinol*. 2016;6(5):460–464. doi:10.1002/alr.21699
32. Huang Y, Wang C, Cao F, et al. Comparison of long-term efficacy of subcutaneous immunotherapy in pediatric and adult patients with allergic rhinitis. *Allergy Asthma Immunol Res*. 2019;11(1):68–78. doi:10.4168/aair.2019.11.1.68
33. Ren L, Wang C, Xi L, et al. Long-term efficacy of HDM-SCIT in pediatric and adult patients with allergic rhinitis. *Allergy Asthma Clin Immunol*. 2023;19(1):20. doi:10.1186/s13223-023-00781-8
34. Shen Z, Tan G, Zhong Z, et al. Interactive network platform improves compliance and efficacy of subcutaneous immunotherapy for patients with allergic rhinitis. *Patient Prefer Adherence*. 2019;13:2101–2110. doi:10.2147/ppa.S235711
35. Dantzer JA, Wood RA. The use of omalizumab in allergen immunotherapy. *Clin Exp Allergy*. 2018;48(3):232–240. doi:10.1111/cea.13084
36. Bozek A, Kozłowska R, Misiołek M, et al. Omalizumab added to allergen immunotherapy increased the effect of therapy in patients with severe local allergic rhinitis. *Hum Vaccin Immunother*. 2022;18(6):2097818. doi:10.1080/21645515.2022.2097818
37. Ridolo E, Nicoletta F, Barone A, et al. Causes of non-adherence to allergen-specific immunotherapy: a foundation towards a patient-personalized approach. *J Pers Med*. 2023;13(8). doi:10.3390/jpm13081206
38. Wang T, Li Y, Wang F, et al. Nonadherence to sublingual immunotherapy in allergic rhinitis: a real-life analysis. *Int Forum Allergy Rhinol*. 2017;7 (4):389–392. doi:10.1002/alr.21909
39. of Rhinology SG. Chinese guideline for diagnosis and treatment of allergic rhinitis (2022, revision). *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2022;57(2):106–129. doi:10.3760/cma.j.cn115330-20211228-00828
40. Langer SS, Cardili RN, Melo JML, et al. Efficacy of house dust mite sublingual immunotherapy in patients with atopic dermatitis: a randomized, double-blind, placebo-controlled trial. *J Allergy Clin Immunol Pract*. 2022;10(2):539–549.e7. doi:10.1016/j.jaip.2021.10.060