

## ORIGINAL ARTICLE

# A national audit of pollen immunotherapy for children in the United Kingdom: patient selection and programme safety

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## Clinical & Experimental Allergy

### Summary

**Background** Specific immunotherapy (SIT) is an effective treatment for grass and/or tree pollen-induced severe allergic rhinoconjunctivitis. However, there are limited detailed data on the use of immunotherapy in children in the United Kingdom.

**Objectives** We audited NHS paediatric practice against current national guidelines to evaluate patient selection, SIT modalities and adverse events (AEs).

**Methods** Paediatricians offering pollen SIT were identified through the British Society of Allergy and Clinical Immunology Paediatric Allergy Group (BSACI-PAG) and the database of SIT providers compiled for the Royal College of Physicians and Royal College of Pathologists 2010 joint working group. Standardized proformas were returned by 12 of 20 centres (60%), including 12 of 14 centres offering subcutaneous immunotherapy (SCIT) (85%).

**Results** Three hundred and twenty-three children, with mean age 11 years at initiation (69% boys), had undergone 528 SIT cycles (SCIT 31%) over 10 years. Fifty-five percent of all patients had asthma. Among SCIT programmes 24.5% patients had perennial ( $\pm$  seasonal) asthma; 75.6% of asthmatics undertaking SCIT had treatments at BTS/SIGN step 2 or above. AEs occurred frequently (50.4% of all SIT cycles) but were mild. In sublingual immunotherapy (SLIT) treatment, local intraoral immediate reactions were most common (44.9% SLIT cycles), as compared with delayed reactions around the injection site in SCIT (28.3% SCIT cycles). An asthma diagnosis had no impact on the number of cycles with AEs, or the severity reported. Few cycles (2.9%) were discontinued as a result of AE(s).

**Conclusions and Clinical Relevance** Pollen SIT is available across England, though small numbers of children are being treated. Current national guidelines to exclude asthmatic children in SIT programmes are not being adhered to by most specialist paediatric allergy centres. SCIT and SLIT has been well tolerated. Review of patient selection criteria is needed and may allow greater use of this therapeutic option in appropriate clinical settings.

**Keywords** asthma, audit, child, immunotherapy, pollen, seasonal allergic rhinoconjunctivitis  
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### Introduction

Seasonal allergic rhinitis (SAR) is a long-term condition that affects up to 15% of children and young people in

the United Kingdom [1] and is most commonly caused by allergy to grass and/or tree pollen. Typical symptoms include sneezing, watery rhinorrhoea, nasal itch and blockage and these may be accompanied by conjunctivitis

and/or wheeze. Furthermore, many patients experience headache, fatigue and poor concentration. Symptoms of SAR can have pervasive effects on sleep, mood and everyday activities, including both attendance and performance at school. These complications can have far-reaching consequences for patients' well-being and social potential [2–5], which may be exacerbated by the use of sedating antihistamines [4, 6]. Allergic rhinitis (AR) frequently coexists with asthma and is a risk factor for its development, particularly in children. Up to 50% of patients with rhinitis have asthma, while rhinitis occurs in up to 80% of patients with asthma [7–9]. This has led to the concept of the unified airway, with evidence that a combined treatment package is needed for optimal symptom control of both conditions [10–14].

Prompt recognition and appropriate medical treatment remain the first-line therapeutic option for affected children, who may require a package of topical (aerosols to the nose and lower airway; eye drops) and systemic (oral antihistamines) medications, together with allergen avoidance advice. Treatments can improve quality-of-life factors [15–18]. Nonetheless, a significant proportion of patients remain symptomatic despite optimal pharmacotherapy [19]. Moreover, children pose particular challenges for treatment, since polypharmacy and inherent need for long-term usage [20] may compromise concordance, while product choices can impact on cognitive ability and academic attainment [4, 21]. There are also potential cumulative adverse effects of topical steroids to nose and bronchi.

The benefit of pollen-specific immunotherapy (SIT) in improving symptoms and quality-of-life and reducing resort to relief medications is well recognized [22, 23]. Moreover, in children with SAR, subcutaneous immunotherapy (SCIT) has been demonstrated to reduce their long-term risk of developing new inhalant sensitizations and asthma [24–26]. However, SIT carries the risk of systemic side-effects and anaphylaxis. Indeed, in 1986 a number of treatment-associated fatalities that had occurred during the previous 34 years were reported [27]. This led to the introduction of stringent operational standards and in the United Kingdom the Committee on Safety of Medicine further advised exclusion of patients with asthma [28]. Since that time a number of sublingual immunotherapy (SLIT) products have been introduced. These have had a favourable safety profile among children, including those with asthma, and thereby offer a home-based therapeutic option [29–31]. Nevertheless, the current (2008) British guidelines on rhinitis management maintain a precautionary stance and advise against SIT in children with asthma irrespective of severity or periodicity [32].

Since 2003, successive reviews from the Royal College of Physicians (RCP), Parliamentary Health committee and House of Lords Science and Technology committee of the

provision of allergy services in the United Kingdom have identified a significant unmet need [33, 34]. Despite these publications, the most recent review has demonstrated that the situation is largely unchanged [35]. The lack of provision of paediatric SIT programmes is compounded further by the dearth of trained specialists. Given that the RCP's 2010 report [35] specifically recommended improving immunotherapy services, we sought to audit paediatric practice in greater detail in order to understand the current scope of this treatment modality. The audit sought primarily to ascertain practitioner adherence to the recommendation that 'SIT is contraindicated in children with asthma' [32]. However, in so doing, we aimed to gather information on which centres are undertaking pollen SIT and how many children have undergone treatment; routes and types of products used; whether treated patients had asthma and the nature of adverse events (AEs) experienced by children undergoing SIT stratified by whether or not they had coexistent asthma. Our hypothesis, based on personal experience, was that with appropriate precautions, as applied in tertiary allergy services, SIT could be safely administered to children with SAR whether or not they had coexistent asthma.

## Methods

Paediatricians providing a pollen SIT service were invited to participate in the audit through the e-mail discussion forum of the British Society of Allergy and Clinical Immunology Paediatric Allergy Group (BSACI-PAG) network. This network is active across the United Kingdom and most paediatricians who are members of the BSACI receive updates by this route. In addition, clinicians who had supplied data about their local SIT practice to the joint Royal College of Physicians (RCP)/Royal College of Pathologists (RCPa) Working Party (formed to produce an update on changes to allergy service provision [35]) were also contacted directly.

Clinicians who expressed an interest in participation were sent the audit proforma. Linked anonymized data on patient demographics, inhalant sensitization profile, year of programme start, SIT product received, asthma status and treatment-related AEs were recorded.

Patient diagnosis and seasonality (perennial and/or seasonal [pollen associated]) of asthma were defined by the local clinician. This diagnosis was based on typical symptoms of recurrent wheeze, where other rarer causes had been excluded, and was substantiated by response to anti-asthma therapy [36]. Treatment requirements, out with and during the pollen season at the start of the SIT programme were categorized according to BTS/SIGN asthma management guidelines [37]. Clinical data on day-to-day symptom control, including measurements of lung function, at the time of SIT treatment were not collected.

Treatment-associated AEs were defined as follows:

- Local: occurring at the site of administration (arm for SCIT; or within mouth for SLIT);
- Systemic: occurring at a distance from the site of administration;
- Immediate: symptoms within 1 h of treatment administration;
- Delayed: symptoms occurring more than 1 h after treatment administration.

The nature of AEs experienced was recorded for each treatment cycle and any requirement for rescue epinephrine. In addition, the outcome of each cycle was documented with respect to programme continuation (programme to continue or completed; programme stopped – related or unrelated to AEs).

Many audit returns, including all those relating to children undergoing SLIT, did not include dose-by-dose detail on AEs. Thus, the AE data are presented with respect to presence and nature of any episode during an individual treatment cycle (cycle refers to a course of subcutaneous injections, or daily oral administrations in 1 year). The number of such episodes is not available.

### Statistical analyses

Descriptive parameters (mean, mode, range, frequency and percentage) were calculated for relevant variables. Pearson  $\chi^2$  or Fisher's exact tests, as appropriate, were applied for categorical data. A probability value of  $P < 0.05$  was considered to be significant. SPSS v17 was used for these analyses.

## Results

### SIT activity

Proformas were returned from 12 centres (Fig. 1). Data were supplied on 323 children who had received one or more cycles of SCIT ( $n = 103$  [31.9%]) or SLIT ( $n = 220$ ) treatment over the past 10 years.

Review of the database of the joint RCP/RCPATH Working Party on paediatric allergy services identified a further eight centres in England and Wales who reported that they offered SIT treatment. This included two centres offering a SCIT programme. Information from four of these remaining centres indicated total numbers of 16 and 22 children who had received one or more cycles/courses of SCIT and SLIT, respectively, although full audit data were not supplied for these children. Thus, the audit contributors (60% of all self-reported practicing centres and 80% of centres undertaking SCIT) supplied data on approximately 86.5% of all children undergoing SCIT and 91% of all children receiving SLIT in England and Wales within an NHS clinic.

Treated children had undergone 528 cycles of immunotherapy, with SLIT route predominating (SCIT:  $n = 165$  [31.3%]; SLIT:  $n = 363$ ). Product types are shown in Table 1. Activity data were supplied by centres for all patients treated. The earliest year of the first treatment cycle was 2000 (three patients) (modal year, 2009).

### Patient selection

Patient age, sex and sensitization status to other inhalant allergens are shown in Table 2.

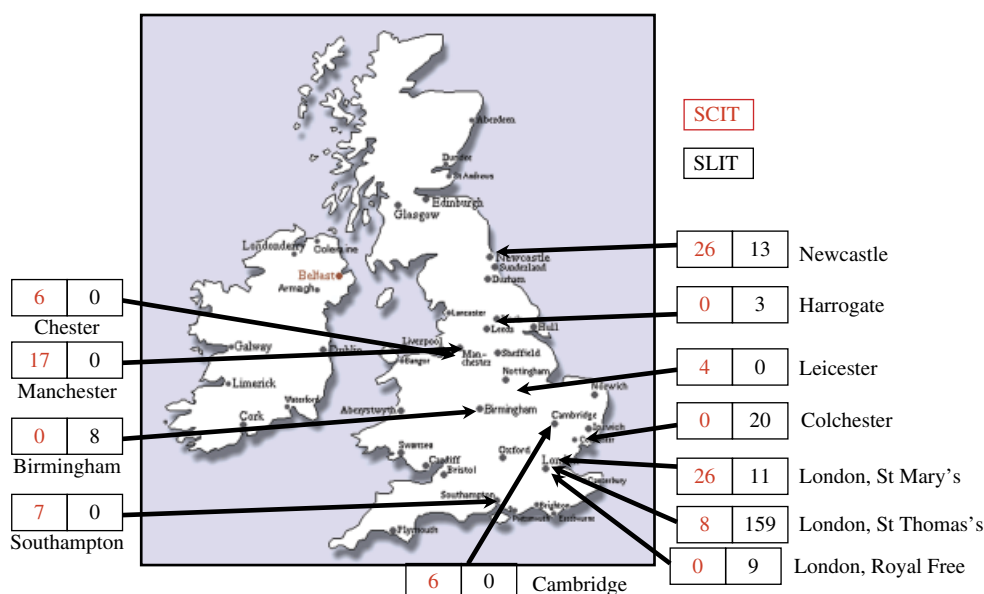


Fig. 1. Centres contributing to audit. The figure shows the NHS allergy clinics that provided audit data. The numbers of patients treated in each centre with subcutaneous (SCIT) and sublingual immunotherapy (SLIT) are indicated.

Table 1. SIT products used

| SCIT ( <i>n</i> = 165 cycles)                         | SLIT ( <i>n</i> = 363 courses)                   |
|-------------------------------------------------------|--------------------------------------------------|
| Pollinex Quattro: 87 [52.7]<br>(Allergy Therapeutics) | Grazax <sup>®</sup> : 110 [30.3]<br>(ALK-Abelló) |
| Pollinex: 52 [31.5] (Allergy Therapeutics)            | Staloral: 253 [69.7]<br>(Stallergenes)           |
| Allergovit: 13 [7.9] (Allergopharma)                  |                                                  |
| Alutard SQ phleum pratense: 13 [7.9]<br>(ALK-Abelló)  |                                                  |

Figures refer to number of cycles (%).

SCIT, approximately 972 injections in total.

SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

Table 2. Patient demographics

|                                                                  | SCIT<br>( <i>n</i> = 165 cycles) | SLIT<br>( <i>n</i> = 363 courses) |               |
|------------------------------------------------------------------|----------------------------------|-----------------------------------|---------------|
| Age, years [mean (range)]                                        | 12.5 (4–18)                      | 10.6 (3–16)                       |               |
| Sex, male [number (%)]                                           | 72 (69.9%)                       | 152 (69.1)                        | <i>P</i> = NS |
| Polysensitized – other<br>inhalant sensitization<br>[number (%)] | 61 (62.9)                        | 110 (65)                          | <i>P</i> = NS |
| Any asthma [number (%)]                                          | 50 (49%)                         | 124 (58%)                         | <i>P</i> = NS |

Data not available for all for inhalant sensitization and asthma diagnosis.

Any asthma refers to children with perennial and/or seasonal symptoms.

NS, not significant; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

## Asthma

Asthma status at SIT initiation was available for 317 (98%) (SCIT: *n* = 102; SLIT: *n* = 215) patients. Fifty-five percent of all patients had perennial and/or seasonal asthma (perennial asthma: *n* = 112 [35.3%]; seasonal asthma only: *n* = 48 [15.1%]; perennial and seasonal asthma: *n* = 14 [4.4%]).

Children undergoing SLIT more often had asthma (*n* = 124 [57.7%];  $\chi^2$ ; *P* < 0.001). This included 101 [47%] with perennial (*n* = 90) ± seasonal asthma (*n* = 11). Among children undergoing subcutaneous immunotherapy, 50 (49%) had asthma, including 25 (24.5%) with perennial (*n* = 22) ± seasonal asthma (*n* = 3). Seven of eight centres offering SCIT and all six centres offering SLIT reported experience of treating children with perennial (± seasonal) asthma.

BTS/SIGN treatment category was available for 49 of 50 children with asthma receiving SCIT and for 122 of 124 asthmatic children receiving SLIT. There were 14 children who had perennial asthma with seasonal worsening (*n* = 11 SLIT; *n* = 3 SCIT) for whom symptom increase was matched by a step-up in treatment in five cases (*n* = 4 increase in inhaled steroids; *n* = 1 addition of montelukast and more frequent salbutamol).

For children undergoing SCIT, 24.4% asthmatic children were receiving step 1 treatment; 42.8% step 2 and 30.6% step 3 asthma therapy. One asthmatic child was on BTS/SIGN step 4 treatment. For asthmatic children

undergoing SLIT, the distribution of BTS/SIGN treatment steps were 16.3% step 1; 40.1% step 2 and 41.8% step 3. Two asthmatic children receiving SLIT were on BTS/SIGN step 4 treatment. Breakdown of BTS/SIGN treatment according to asthma category is shown in Figs 2a and b.

## Adverse events

Data on AEs were available for all SIT cycles. Two hundred and sixty-six (50.4%) SIT cycles were complicated by one or more AEs. Reactions were as common in SLIT cycles as SCIT courses (SLIT: 192/363 cycles, 52.9%; SCIT: 74/165, 44.8%;  $\chi^2$ ; *P* = 0.087). AEs described in SCIT cycles were most commonly either local delayed (30/74; 40.5%) or systemic delayed reactions (21/74; 28.3%) only. On the other hand, local immediate symptoms predominated among AEs in SLIT cycles (146/192; 76%). Other combinations of local, systemic, immediate and delayed events were described (Figs 3a and b).

The nature of events described and event type as a proportion of all treatment cycles are shown for each SIT modality in Fig. 4. Local immediate reactions (itchy mouth, throat, ears, nose; intraoral swelling and taste aversion) were by far the most common adverse symptoms found in SLIT treatment, affecting 44.9% of all SLIT cycles. Gastrointestinal upset was the most common systemic symptom (8% SLIT cycles). On the other hand, children receiving SCIT most frequently developed swelling around the injection site and had local pain, redness, itch or tenderness (26.1% SCIT cycles). One or more episodes of rhinitis, conjunctivitis, or malaise and 'flu-like' symptoms affected 9.7% and 8.5% of SCIT cycles, respectively. 'Other' treatment-associated AEs included individual cases of nose/gum bleed, dizziness, itchy head and increased frequency of absence seizures. A causal relationship with SIT is unlikely but these have been included to provide a complete list of AEs. Details of reactions with reported respiratory symptoms are summarized in Table 3. No centre reported use of epinephrine in treatment of reactions.

Both AE data and asthma category were available for 521 (98.7%) cycles. Among the whole cohort, SCIT and SLIT subgroups, there were no significant differences in the number of cycles affected by one or more AEs in those with asthma as compared with those without asthma. In the whole cohort there was at least one AE in 99/188 (52.7%) cycles in perennial asthmatics; 35/75 cycles (46.7%) in seasonal asthmatics; 10/28 (35.7%) cycles in perennial and seasonal asthmatics; and 118/230 (51.3%) cycles in non-asthmatics. For subcutaneous immunotherapy, 38/84 (45%) of cycles in non-asthmatic patients were complicated by 1 or more AEs. This compared with 14/37 (38%) of cycles in perennial asthmatics; 18/38 (47%) cycles in seasonal asthmatics and 3/5 (60%) of cycles in perennial asthmatics who had seasonal worsening ( $\chi^2$ ; *P* = 0.730). Similarly, 80/146 (55%) cycles in non-asthmatic children receiving SLIT had one or more AEs, while

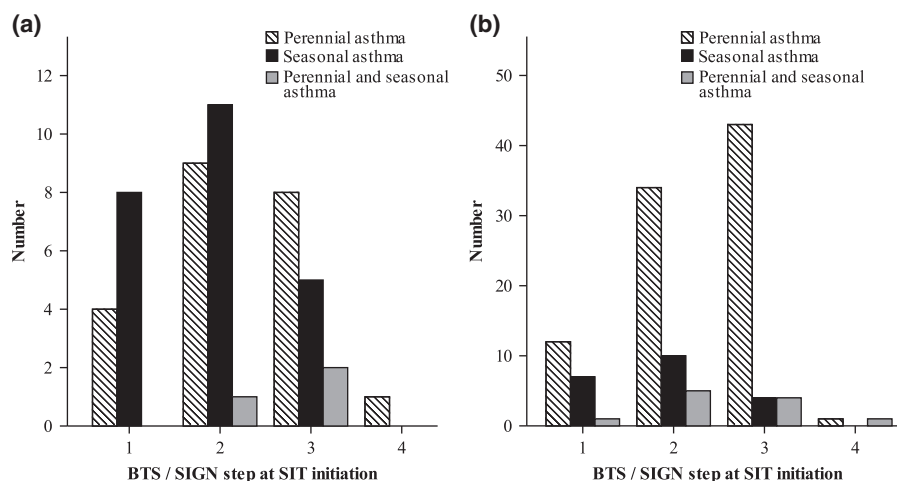


Fig. 2. (a) Asthmatic children according to BTS/SIGN treatment steps: subcutaneous immunotherapy (SCIT) programme. The figure shows the number of asthmatic children (perennial, seasonal, perennial with seasonal worsening) receiving SCIT according to their individual baseline BTS/SIGN asthma treatment step. (b) Asthmatic children according to BTS/SIGN treatment steps: sublingual immunotherapy (SLIT) programme. The figure shows the number of asthmatic children (perennial, seasonal, perennial with seasonal worsening) receiving SLIT according to their individual baseline BTS/SIGN asthma treatment step.

109/211 (51.7%) cycles in all asthmatic children (perennial, seasonal, perennial with seasonal worsening) had treatment-associated AE(s) ( $\chi^2$ ;  $P=0.099$ ). The range of AEs was seen in all asthma categories (Figs 5a and b). In SCIT programmes only seven cycles were associated with some form of respiratory symptom; five were in children with seasonal asthma and two in children with perennial asthma (Table 3).

### Outcomes

Cycle outcome (continuing/completed or stopped) was available for 525 (99%) cycles. Programme drop-out rate was low with treatment discontinuation in only 28 cycles (5.4%), of which 15 (2.9%) ( $n=6$ , 3.7% SCIT;  $n=9$ , 2.5% SLIT) related to AEs experienced.

Of the six patients who discontinued SCIT, in four cases this was a result of respiratory compromise. This included two children who experienced a wheezy episode 12–24 h after therapy. One of these children also had rhinitis, malaise/flu-like symptoms and local swelling, which also contributed to the decision to stop therapy. Of the two children who stopped treatment because of acute bronchospasm, one child re-started SCIT therapy (with same product) the following year and thereafter completed the full course. In the main, children discontinued SLIT due to poor tolerance of local (oral) symptoms. One child discontinued because of persistent, immediate-onset abdominal pain, vomiting, wheeze and headache.

### Discussion

This is the first national audit of paediatric pollen immunotherapy practice in the United Kingdom. The data do not

include those older children/adolescents who may have undergone pollen desensitization in adult allergy clinics or in the private sector, as our intention was to focus on the approach to treatment and AE experiences of paediatric practitioners within NHS clinics only. The BSACI-PAG e-mail network was used initially to highlight the audit and request centre participation. While this forum is accessible across the United Kingdom, it requires individual voluntary registration. Accordingly, a second, direct invitation to participate was made using a database of paediatric allergy centres/clinics in England and Wales compiled for the Royal College of Physicians and Royal College of Pathologists 2010 joint working group [35]. While the audit failed to capture data from every NHS site offering pollen SIT, the small total numbers of treated patients reported by non-contributing centres suggests that this audit is representative of the vast majority of paediatric NHS SIT activity in England and Wales.

With the exception of one London clinic, which had a large SLIT cohort, most centres had treated relatively small numbers of children. This reinforces the need for, and benefit of a national audit of this kind to facilitate sharing of clinical experience, review and update of good practice guidelines.

As part of this audit we aimed to explore practitioner adherence to the current national recommendation that 'SIT is contraindicated in children with asthma' [32]. However, we were also aware that several centres were not excluding children with co-existent asthma. Our findings indicate that the guideline on SIT in asthma is not being followed in the vast majority of centres: 55% of children undergoing SIT had asthma, which included 39.7% with perennial  $\pm$  seasonal asthma. This approach applied to both types of SIT: 47% of SLIT patients had

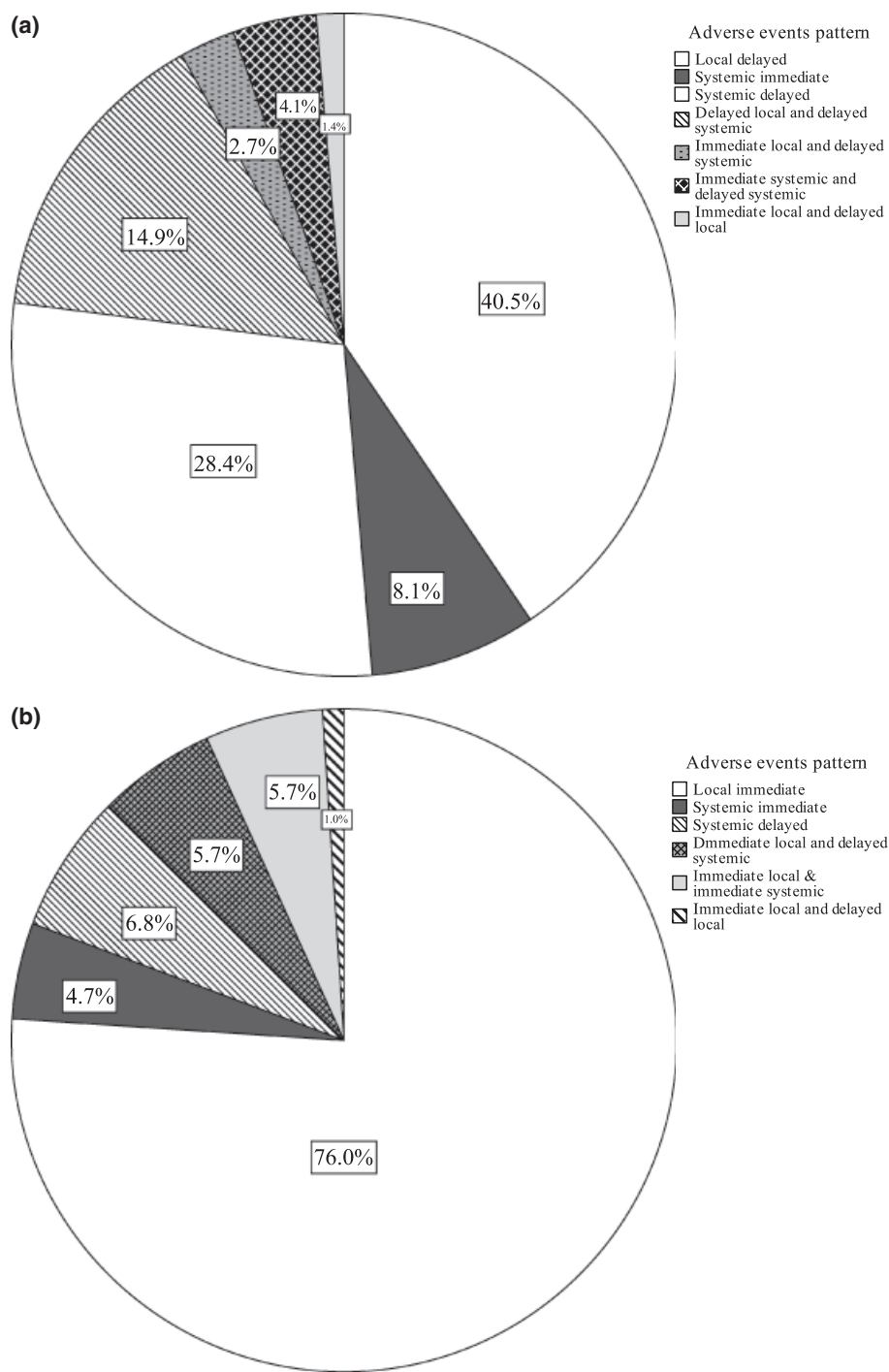


Fig. 3. (a) Adverse event (AE) patterns: subcutaneous immunotherapy (SCIT). The figure shows the proportion of all AEs occurring in SCIT programmes according to the event categories – local or systemic and immediate or delayed. (b) AE patterns: sublingual immunotherapy (SLIT). The figure shows the proportion of all AEs occurring in SLIT programmes according to the event categories – local or systemic and immediate or delayed.

perennial asthma as compared with 24.5% of subcutaneous immunotherapy patients.

Asthma presence and type (perennial; seasonal) were recorded by the local practitioner. Accuracy of categorization is supported by the observations that children with perennial asthma were more often polysensitized to

airborne allergens ( $\chi^2$ ;  $P=0.004$ , data not shown) and had higher treatment requirements (BTS/SIGN step) ( $\chi^2$ ;  $P=0.01$ , data not shown).

Asthma has posed understandable concern for allergen desensitization practice since a high proportion of SCIT-associated fatalities have been linked to poorly controlled

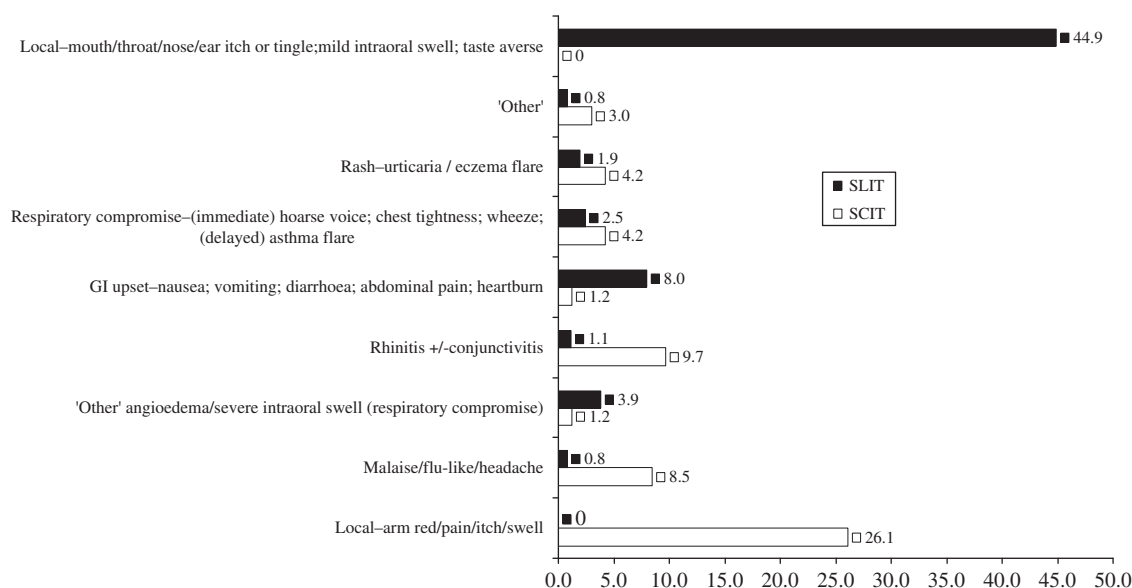


Fig. 4. Nature of adverse events (AEs): all cycles subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT). The figure shows the nature of AEs and the respective percentage of all immunotherapy cycles affected.

Table 3. Respiratory reactions in detail

| Number | SIT type | Reaction                                                                                                                  |
|--------|----------|---------------------------------------------------------------------------------------------------------------------------|
| 1      | SCIT     | Perennial asthmatic. Mild asthma exacerbation starting 24–48 h after third dose. Required oral steroid. Programme stopped |
| 2      | SCIT     | Seasonal asthmatic. Delayed onset rhinitis and reduced peak flow after fourth dose. Programme continued                   |
| 3      | SCIT     | Perennial asthmatic. Acute onset wheeze after dose. Programme stopped                                                     |
| 4      | SCIT     | Seasonal asthmatic. Delayed onset wheeze, cough, rhinitis, flu-like symptoms. Programme stopped                           |
| 5*     | SCIT     | Seasonal asthmatic. Immediate onset wheeze. Cycle stopped. Restarted following year                                       |
| 6*     | SCIT     | Seasonal asthmatic. Immediate onset wheeze. Cycle continued                                                               |
| 7      | SCIT     | Seasonal asthmatic. Immediate chest pain. Course continued                                                                |
| 8      | SLIT     | Seasonal asthmatic. Throat tight. Hoarse voice. Course continued                                                          |
| 9      | SLIT     | No asthma. Throat tight. Hoarse voice. Course continued                                                                   |
| 10     | SLIT     | Seasonal asthma. Change in voice. Course continued                                                                        |
| 11     | SLIT     | Perennial asthma (seasonal worsen). Acute wheeze, GI upset, headache. Programme stopped                                   |
| 12     | SLIT     | Perennial asthma. Chest pain. Dizzy. Course continued                                                                     |
| 13     | SLIT     | No asthma status given. 'Breathing difficulty' (not defined). Course continued                                            |
| 14     | SLIT     | Perennial asthma. Cough. Course continued                                                                                 |
| 15     | SLIT     | Perennial asthma. Cough. Course continued                                                                                 |
| 16     | SLIT     | Perennial asthma. Increased asthma symptoms. Course continued                                                             |

\*Same patient.

GI, gastro-intestinal; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy.

asthma [27, 38]. A more favourable safety profile for SLIT, with reduced risk of systemic AEs, has been established in children, including those with mild asthma and/or exclusive seasonal symptoms [30, 31]. Notably, in this audit, over 90% of all asthmatic patients undergoing SIT were maintained on regular inhaled steroids. The distribution of patient treatment requirements (BTS/SIGN steps) were similar in both SCIT and SLIT groups. While we did not collect details of lung function testing, or asthma symptoms during and outwith the pollen season, nonetheless BTS/SIGN step at SIT initiation defines treatments needed

to maintain overall symptom control and thereby gives an indication of severity. Thus, paediatric allergists are opting to offer pollen immunotherapy to children with asthma, including those with moderately severe disease.

Given patient selection that included asthmatic children, the AE data assumes particular importance. It presented the opportunity to address our hypothesis that in specialist centres SIT could be administered as safely to children with or without asthma. Overall, AEs occurred commonly in this cohort with approximately 50% of all cycles being affected by at least 1 event. For both

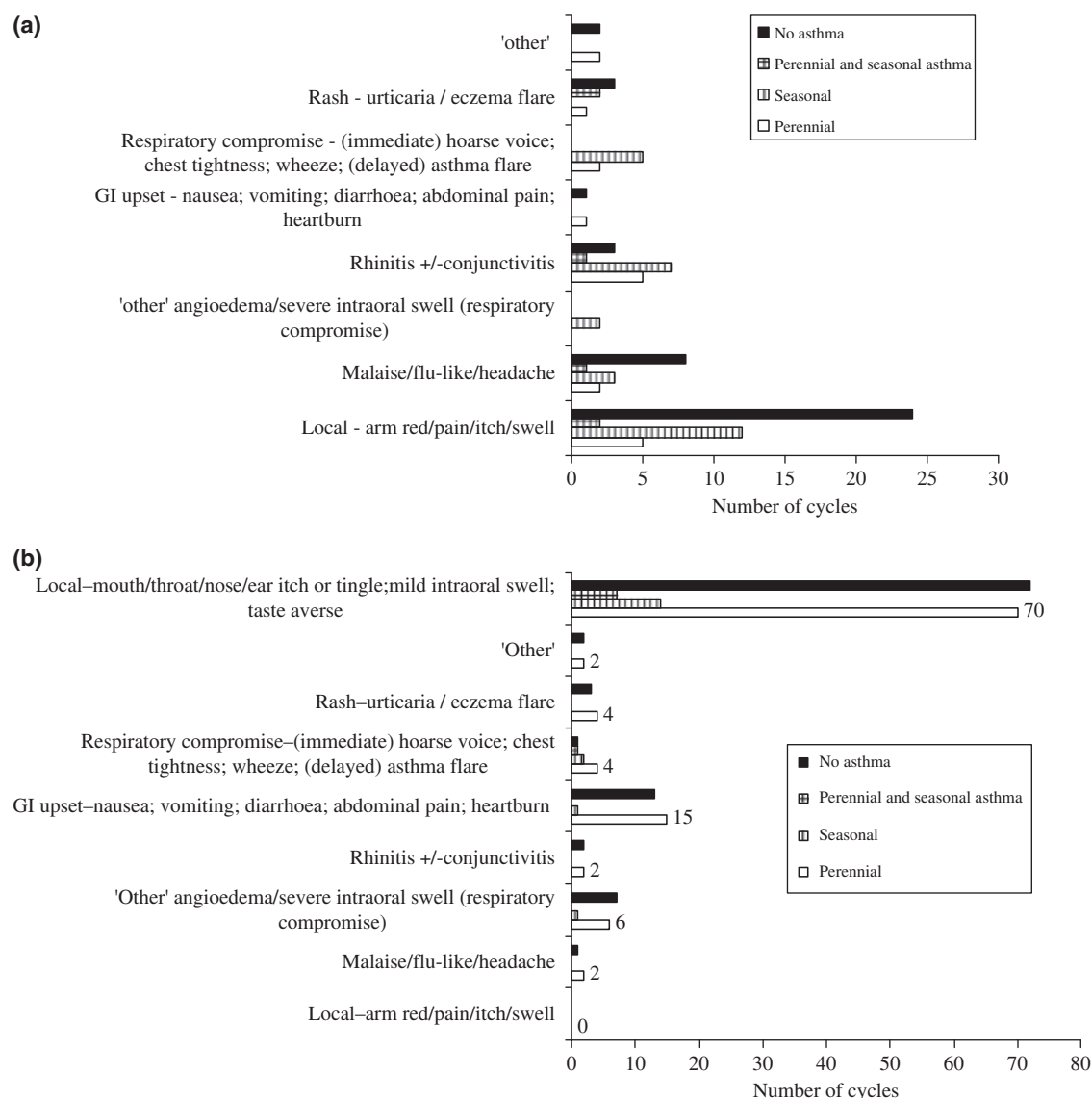


Fig. 5. (a) Subcutaneous immunotherapy (SCIT): nature of adverse events (AE) according to asthma category. The figure shows the nature of AEs and the respective number of subcutaneous cycles (SCIT) affected according to asthma status. (b) Sublingual immunotherapy (SLIT): nature of AE according to asthma category. The figure shows the nature of AEs and the respective number of sublingual courses (SLIT) affected according to asthma status.

treatment modalities, local reactions at or near the injection/application site occurred most frequently. For SLIT, immediate intraoral (ear or nose) itch or swelling was the most common single AE, constituting 76% of all SLIT-associated events and occurring in approximately 45% (alone or in combination) of SLIT cycles. Likewise for SCIT, delayed swelling, pain or itch occurred most commonly, affecting approximately 26% of all SCIT cycles. Both treatments were associated with a number of additional effects. Gastrointestinal upset has been observed previously with SLIT in children [29, 30] and similarly in this audit it was the second most common AE, occurring in 8% of cycles (alone or in combination). Among SCIT cycles, mild rhinitis and general malaise were the most

common systemic effects. Our findings related to AE are broadly in line with previously published data related to tolerance of SIT in paediatric patients [29–31, 39, 40].

The presence of co-existent asthma, or asthma type (perennial, seasonal) had no impact on the number of cycles with a reported AE or severity of the events described. While this is reassuring, we acknowledge that the findings relate to a relatively small number of patients. Furthermore, the detail on treatment-associated adverse reactions in children, and the impact of asthma diagnosis, is limited by paucity of data on dose-by-dose events. Notwithstanding this, it is encouraging that over 970 injections were given without serious side effect. No reported AE required use of adrenalin/epinephrine. Moreover, the very low drop out rate (2.5% SLIT; 3.7% SCIT)

suggests that the local and systemic events reported were tolerable to the children undergoing treatment.

The current UK recommendation is that children with asthma should not undergo immunotherapy for AR [32]. Up to 50% of patients with AR may also have asthma [48], and allergen SIT may have benefit for asthma symptoms [30, 41, 42]. The recommendations therefore exclude a large number of children who might otherwise have considerable clinical benefit from a 'unified airway' approach. The current audit offers some reassurance that SIT can be administered safely in asthmatic children. However, our audit conclusions are based on relatively small numbers of patients and we would emphasize a need for careful selection of children with well-controlled asthma and treatment administration in line with nationally agreed standard operating procedures, which for SCIT means observation for at least 1 h after each dose and the immediate availability of full-resuscitation facilities, in order to maintain the impressive safety record of recent years [22, 23, 43].

The clinical implication of this work is that there is likely an 'Unmet Need' for allergen-SIT treatment of children with severe AR, whose lives are affected significantly by the condition. We believe that we have identified the majority of children receiving this modality of treatment in the United Kingdom. Given the prevalence of SAR this is a very low percentage of those likely to benefit. Currently SIT is the only treatment that improves the long-term natural history of AR, with reduction in symptoms and medication use [22, 23, 26]. Moreover, SIT has been demonstrated to reduce the development of new inhalant sensitization [26, 44] and also the progression of rhinitis to asthma [24–26]. In the current study, only 323 children had been treated across centres in England over the last 10 years. To put this into perspective: a previous survey of adult patients with AR in primary care suggested that 27% used maximal therapy, yet almost 15% of this group remained symptomatic despite optimal medication use, and thus might be eligible for SIT [19]. Given that 10% and 15% of children aged 6–7 and 13–14 years, respectively, in the United Kingdom have AR [1], if these adult figures are extrapolated to the whole paediatric population in England and Wales (Office of National Statistics, 2001: 8 063 119 children aged 5–16 [45]), we

can estimate crudely that over 32 000 children could be considered suitable for immunotherapy. In other words, we are treating only 1% of affected patients, with consequent cost to child, family and society [46, 47]. We recommend that it is timely to develop paediatric-focused guidelines for allergen immunotherapy, supported by regular re-audits, which may improve access to this treatment by a wider number of eligible patients. Future research should address symptom severity and control among children with SAR such that we can understand fully the 'Unmet Need' of this therapy.

Children undergoing pollen SIT in the United Kingdom have tolerated the treatment well with no serious AEs described over the last 10 years. There is a need for an urgent review of service provision such that we can offer the best possible clinical care to our paediatric patients.

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