The British Society for Allergy & Clinical Immunology

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First BSACI Registry for Immunotherapy Report

2020

Prepared by

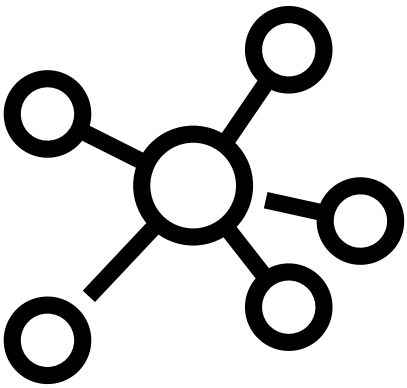
Michel Erlewyn-Lajeunesse DM FRCPCH

on behalf of The British Society for Allergy & Clinical Immunology

Peter Walton MBA FRCP
Robin Kinsman BSc PhD

Dendrite Clinical Systems Ltd

The British Society for
Allergy & Clinical Immunology



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The British Society for Allergy & Clinical Immunology operates the Registry for Allergy & Clinical Immunology in partnership with Dendrite Clinical Systems Limited. The Society gratefully acknowledges the assistance of Dendrite Clinical Systems for:

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The British Society for Allergy & Clinical Immunology

The British Society for Allergy and Clinical Immunology (BSACI) is the national, professional and academic society, which represents the specialty of allergy at all levels. Its aim is to improve the management of allergies and related diseases of the immune system in the United Kingdom, through education, training and research.

BSACI
Improving Allergy Care
through education, training and research

Our sponsors

We would like to thank:

ALK Abello, Allergy Therapeutics and Stallergenes Greer who have funded the development of the Registry with unrestricted educational grants to BSACI.

ALK

Allergy Therapeutics PLC

STALLERGENES GREER

Patient participation

We would like to thank Lynne Regent CEO of the Anaphylaxis Campaign and Amena Warner and Carla Jones CEO of Allergy UK for their support of the Registry.

AllergyUK

Anaphylaxis Campaign
Supporting people at risk of severe allergies

Quality standards

BRIT is recommended by IQAS, the allergy quality standards unit of the Royal College of Physicians.

Royal College of Physicians | Improving Quality in Allergy Services

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- Dr Shuaib Nasser

The current BSACI Registry Steering Committee:

- Dr Tom Dawson
- Dr Sujoy Khan
- Dr Anna Thursby-Pelham
- Dr Deborah Marriage
- Dr Leyla Pur
- Dr Louise Michaelis

and our co-opted members

- Lynne Regent, Anphylaxis Campaign,
- Carla Jones, Allergy United Kingdom
- Prof. Thirumala Krishna, IQAS

Glossary

AE	Adverse Event
AEFI	Adverse Event Following Immunisation
AIT	Allergen Immunotherapy
AR	Adverse Reaction
BC	Brighton Collaboration
BRIT	BSACI Registry for Immunotherapy
BTS	British Thoracic Society
CSU	Chronic Spontaneous Urticaria
GP	General Practitioner
HCP	Health Care Professional
ICS	Inhaled Cortico Steroids
ICSR	Individual Case Safety Report
IT	Immunotherapy
MAB	Monoclonal Antibody
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare Regulatory Agency
OMA	Omalizumab
PROM	Patient Reported Outcome Measure
RSC	Registry Steering Committee
SAE	Serious Adverse Event
SCIT	Subcutaneous Immunotherapy
SIT	Specific Immunotherapy
SLIT	Sub-lingual Immunotherapy
VIT	Venom Immunotherapy
WAO	World Allergy Organization

Forewords

Prof. Adam Fox, President, BSACI, says:

We can do more for our patients when we work together. It has long been acknowledged that immunotherapy, despite being a highly efficacious treatment, is underused in the United Kingdom and we have a large, unserved group of patients with a significant burden of unnecessary disease. If we are going to convince commissioners of this need and bring about genuine change for our patients then there are a number of tasks we have to fulfil. Research, through large scale randomised controlled trials and systematic reviews, have already done the job of proving the efficacy of immunotherapy but it is only through real world evidence of acceptability, safety and effectiveness that we will have the tools that we need. There is, of course, some value in the data collected from single specialist centres but when we come together to form registries such as BRIT and develop a true community of practitioners from across the country in both specialist and non-specialist environment, then we have far greater power. The BRIT registry is an extraordinarily important opportunity to harness this power for the good of our patients and it is critical that we all see it as our responsibility to play a role in this. This report is a fantastic start at demonstrating just what we can achieve. I look forward to all of us being active contributors to what will no doubt be considered, in a few years' time when we look back, as a real watershed moment for our specialty. I would like to pay tribute to Mich Lajeunesse for his innovative thinking, persistence and leadership in making this happen and assure him of the full support of the BSACI in this wholly worthwhile endeavour.

Lynne Regent, CEO of the Anaphylaxis Campaign says:

The Anaphylaxis Campaign fully supports the BRIT patient registry as an essential tool in ensuring that patients' immunotherapy treatment is recorded to enable review of effectiveness and the monitoring of adverse effects to ensure patient safety, thereby allowing for further developments. The continued advancement of immunotherapy for the allergic population offers hope that their allergic symptoms can be minimised thereby improving their quality-of-life.

Prof. M Thirumala Krishna, Clinical Lead, IQAS, RCP accreditation units says:

Research in the last two decades has highlighted the importance of immune-modulatory therapies for immune-mediated disorders including asthma and allergy. The establishment of the BRIT registry by the BSACI is an important step in this regard and is a part of its long-term strategy in the delivery of a safe, equitable and standardised care with respect to immune-modulatory therapies delivered by allergists. The BSACI and RCP accreditation unit are collaborating on this important project and commitment to the BRIT registry is embedded in the recent iteration of IQAS standards. Importantly, the establishment of such a registry will enable generation of much needed national level data for the United Kingdom NHS and commissioners.

Carla Jones, CEO Allergy UK says:

Allergy UK, an information and support patient charity is pleased to be an inclusive partner in the BRIT registry project. Immunotherapy in the United Kingdom is underused. Collecting quality data within a registry framework is key to providing real-life usage and metrics from this game-changing treatment.

Executive summary

- The BSACI Registry for Immunotherapy (BRIT) was launched in October 2018. It is an on-line national registry for patients receiving allergen immunotherapy (AIT) to aeroallergens and venom, as well as omalizumab for chronic urticaria.
- Its aim is to describe treatments and services, and monitor the safety and clinical effectiveness of treatment.
- The registry has grown steadily since its launch and by May 2020 had 101 registered consultant users from 65 different centres, with an additional 76 delegate-users, mainly nurse specialists and junior doctors.
- There were 580 participants, the vast majority from England, both inside and outside the greater London area. There were no participants from Scotland nor any from Northern Ireland.
- 96% of participants had agreed to email contact with the registry to return quality-of-life data during and after treatment.
- 455 were receiving aeroallergen allergen immunotherapy for seasonal and perennial allergic rhinitis with grass pollen, tree pollen and house dust mite the most common allergens treated.
- 99% allergen immunotherapy patients had prior testing to confirm the allergens to be used for treatment.
- Sub-lingual immunotherapy was the treatment route in 84% of allergen immunotherapy participants.
- Asthma is a relative contraindication for allergen immunotherapy. 160/455 participants had asthma with 31% treated at British Thoracic Society (BTS) step 3 or above.
- Of the 50 cases that had stopped allergen immunotherapy, only 9 reported that this was for a reason other than the completion of the treatment course. Four were related to poor adherence (SLIT) and 5 for side effects. Only one episode of anaphylaxis was reported.
- 103 participants received venom immunotherapy (VIT), the majority for moderate or severe allergic reactions to stings. Reaction to wasp venom was more common amongst the participants than reaction to bee venom by a ratio of 2:1.
- There were 23 field stings reported to the registry during the course of venom immunotherapy and 273 no-sting reports. Only one participant reported an allergic reaction to a field sting, but they did not require adrenaline.
- 20 participants were registered for omalizumab treatment for Chronic Spontaneous Urticaria (CSU). In keeping with NICE guidelines all these participants had received high dose H1 antihistamine before treatment.
- Patient Reported Outcome Measures have been recorded for allergen immunotherapy and venom immunotherapy and CSU, both during and after immunotherapy. Further analysis of these data are required.
- BRIT is being rapidly adopted by immunotherapy centres across the United Kingdom and will provide an overview of treatment safety and effectiveness in the coming years.

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Introduction

Immunotherapy is a broad term that covers a range of treatments that modulate the immune response. Several treatments are routinely used by allergy specialists in the United Kingdom, these include allergen immunotherapy (AIT) to common environmental allergens such as grass and house dust mite, and venom immunotherapy (VIT) for those who have experienced systemic allergic reaction to insect stings [1, 2]. Immune modulation using anti-immunoglobulin E (Omalizumab, OMA) is also routinely used by society members for the treatment of Chronic Spontaneous Urticaria (CSU) [3].

There are fewer allergy specialists in the United Kingdom than other developed countries leading to an *unmet need* for specialist care [4]. Most immunotherapy is limited to specialist allergy centres in the United Kingdom. Practice differs elsewhere in Europe where immunotherapy is supervised by office-based allergy specialists funded privately or through private medical insurance rather than by state funded treatment.

In consequence, immunotherapy is much less accessible in the United Kingdom than in other European countries, and despite state funding free at point of care, is likely to have led to inequity of access to treatment [5]. Due to the restriction around public funding of immunotherapy, most specialist centres manage only a handful of patients. It is difficult to gain sufficient numbers to draw meaningful conclusions about the safety and effectiveness of treatment or to benchmark personal practice against national trends.

A participant registry is a type of observational study that allows collection of data about patients who have a common disease or have received certain treatments [6]. Web-based patient registries are a well-tested way of collecting data on the real world use of specialist treatments [7]. They have been used successfully in a range of clinical settings where they have the potential to transform standards of care [8].

The BSACI Registry for Immunotherapy (BRIT) was launched in October 2018. This is the first report from the registry, a snapshot at 18 months.

The BSACI registry

Aims and objectives

The registry records episodes of treatment for:

1. Allergen immunotherapy (AIT) both subcutaneous and sub-lingual immunotherapy (SCIT and SLIT).
2. Venom immunotherapy (VIT).
3. The use of the monoclonal antibody Omalizumab (OMA) for Chronic Spontaneous Urticaria (CSU).

Primary objectives

To describe the real-world use of immunotherapy for both adults and children in the United Kingdom, regarding:

A. The clinical use of immunotherapy.
B. The safety of immunotherapy.
C. The reasons for stopping of immunotherapy.
D. The effectiveness of immunotherapy both during and after treatment.

Secondary objectives

E. To describe access to immunotherapy across the United Kingdom and the effect of location and socio-demographic factors.
F. To improve standards of care for patients treated with immunotherapy in the United Kingdom.

Principles of the registry

In order for a registry to flourish the data collected must be of direct relevance to the people involved in its submission. Registry data should also be accessible to all those involved. There are three overriding principles that govern this registry.

The BRIT principles are:

1. We work in partnership with our patients: data are only collected with the express written consent of the participant. We rely on working in partnership with our participants for long-term follow up of their outcomes to help us and others like them. Each participant has a timeline page that summarises their treatment, adverse reactions and Patient Reported Outcome Measures (PROM) data as a useful clinical summary. At present the timeline and participant details can not be directly accessed by the participant, but they can be accessed and shared easily by their consultant or their delegated user.
2. We work in partnership with the healthcare users: each consultant has access to the data on their own patients and service; the data can be easily accessed for immediate download from the registry. This will help with clinical care, local audit and service evaluation and the accreditation of allergy services through IQAS.
3. We only collect data where it serves a purpose. We do not ask for data without a good reason for doing so, such as to meet the aims and objectives of the registry and to show compliance with current BSACI guidelines. This keeps the database lean and makes it as easy as possible to enter clinically relevant data.

Configuring clinics in the registry

The registry is open to all adults and children receiving immunotherapy under the care of a BSACI consultant-grade practitioner working in the United Kingdom.

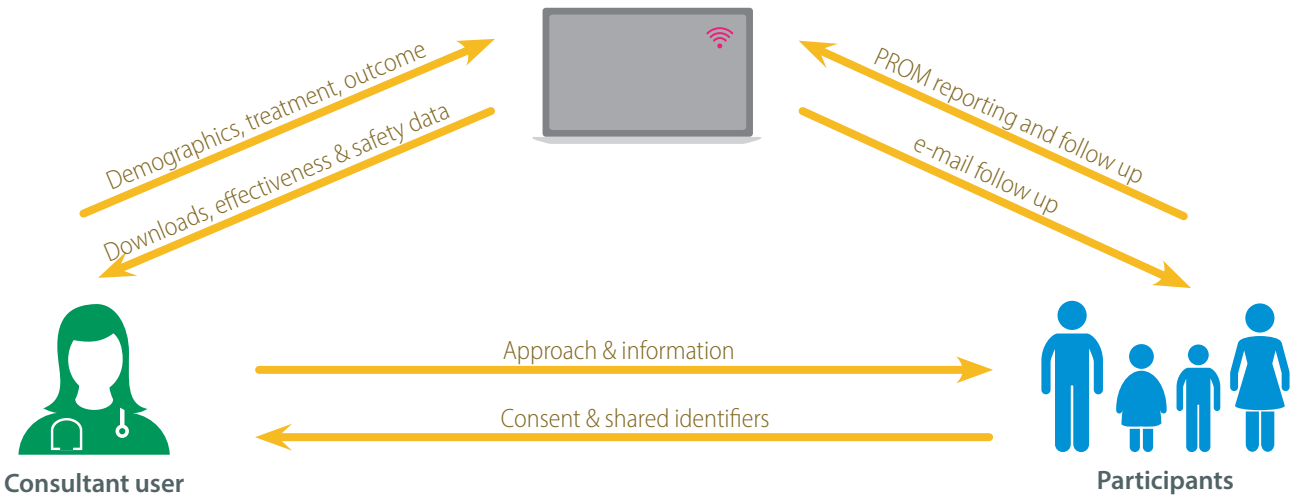
Healthcare users are able to work in teams to view data on participants where there is shared care. Each team must have at least one consultant grade user in order to access the registry. For governance purposes the consultant must be a member of BSACI. If there is more than one consultant in the team, they can arrange to share access to their patients' data.

Consultant users are able to delegate data entry to other members of their team; for instance junior doctors, nurse specialists and clerical staff.

A consultant can include their practice from several different hospitals and clinics under a single consultant user account. They can include both NHS and private-based care.

Registry design

BRIT is a web-based registry that can be accessed using a standard web browser, allowing users to enter data without the need to install additional software or perform any complex system configurations. The system allows the clinicians to enter patient information onto a database whether in hospital or from an office-based practice, and will allow access to the registry for both NHS and private practice users.



Participant enrolment

Patients are asked to join the registry by their supervising consultant or a delegated user such as the nurse specialist running the immunotherapy clinic. There are a range of tailored participant information leaflets aimed specifically at children and adults. Participants must provide written consent to join the registry. There are specific consent forms available for this purpose, for adult patients and for parents / legal guardians of paediatric patients. Signed consent forms should be kept in the patient medical notes but do not need to be sent to BSACI. Consent is required because the registry collects personal identifiable information and also seeks to engage the participant in monitoring their own care by the completion of regular online Patient Reported Outcome Measures (PROM) forms. Participants or their parents / legal guardians can then be contacted by the registry at intervals to record effectiveness data.

What standards have been used?

Information about immunotherapy episodes is recorded according to current United Kingdom guidelines:

- AIT 2017 https://www.bsaci.org/wp-content/uploads/2020/01/Scadding_et_al-2017-Clinical_amp_Experimental_Allergy.pdf.
- VIT 2011 http://www.bsaci.org/guidelines/venom-allergy.
- CSU 2015 (2e) http://www.bsaci.org/guidelines/chronic-urticaria-and-angioedema.
- Omalizumab for CSU TA 339 2015 https://vwww.nice.org.uk/guidance/ta339.

In this way using the registry benchmarks the service against current best practice.

Measures of real-world effectiveness

Effectiveness is assessed by validated Patient Reported Outcome Measures (PROM). These are either completed by hand in a clinic or can be automated and sent to the participant by e-mail at intervals (see table). Participants must agree to sharing their email with the registry for this to happen.

PROMs used in the BRIT registry

	Child under 16	Adult over 16
Allergen immunotherapy	• Paediatric Allergic Disease Quality of Life (PADQLQ)[9]	• Rhinitis Quality of Life Questionnaire (RQLQ)[10]
Venom immunotherapy	• BRIT Field Sting Questionnaire (BRIT FSQ)	• BRIT Field Sting Questionnaire (BRIT FSQ)
	• Venom Quality of Life Questionnaire (VQLQ)[11]	• Venom Quality of Life Questionnaire (VQLQ)[11]
Omalizumab	• Urticaria control test (UCT)[12]	• Urticaria control test (UCT)[12]
	• Children's DLQI[13]	• Dermatology Life Quality Index (DLQI)[14]

Do we need to record every injection?

Consultants only record clinical and treatment data at the start of a course of immunotherapy and at the end of treatment. So, for a subcutaneous course of treatment, that's the first injection and the last, and the registry assumes standard patterns of treatment in between.

What happens at the end of treatment?

Reasons for the end of treatment are recorded to collect both patient-focused reasons and adverse reaction / side effect data leading to stopping therapy [15]. Consultants can report serious adverse events and adverse reactions leading to discontinuation of treatment.

At the end of treatment participants are offered an opportunity to enrol in long-term follow up of treatment efficacy using regular email questionnaires. This provides an opportunity to assess the long-term effectiveness of treatment.

Adverse event reporting

BRIT has the ability to record the safety of treatment in the United Kingdom. Users should report:

1. Any Adverse Event (AE) that leads to the discontinuation of immunotherapy.
2. All Serious Adverse Events (SAE).

Serious adverse events and deaths from immunotherapy are very rare, although they have occurred historically. Notification of such an event will trigger a *rare event tracker* within the registry. The tracker will automatically report the death to the Registry Steering Committee by e-mail for urgent review in discussion with the participant's consultant, who will then inform the MHRA and the holder of the Marketing Authorisation.

The registry uses standard definitions from the Medical Dictionary for Regulatory Activities (MedDRA) that allow direct comparison with international pharmacovigilance data [16]. Causality assessment will follow standard Research Adverse Event reporting and MHRA Yellow Card practice. We are working towards enabling consultants to create an Individual Case Safety Report (ICSR) from the data entered in the registry, and then submit these reports electronically to the competent authority (MHRA Yellow Card Scheme) and Marketing Authorisation Holder (MAH) using a standard registry-generated report in line with Eudravigillance Good Pharmacovigilance Practice [17]. The ICSR will be anonymous (the patient is only identifiable by their unique BRIT number) and include an identifiable reporting clinician with contact details, the suspect drug, details of the adverse event using MedDRA terms and a determination of the seriousness of the SAE. Although the registry is anonymous, the report will be identifiable to the local consultant who has access to a separate log of how the BRIT unique identifiers relate their named patients.

The registry is able to record several different types of adverse event.

- Injection site symptoms.
- Oral symptoms.
- Systemic adverse reaction.
- Suspected anaphylaxis.

Severity grading of allergic reactions follow World Allergy Organisation (WAO) grading for SLIT and the Brighton Collaboration (BC) definition for Anaphylaxis as an Adverse Event Following Immunisation (AEFI) [18-20]. Unlike other anaphylaxis definitions the BC definition has an advantage in that it does not contain causality assessment yet maintains accuracy [21]. Local injection site or application site reactions use the Brighton Collaboration Local Injection Site Reaction definition at level 1; namely, a *morphological or physiological change at the injection [or application] site that has been described and identified by a healthcare provider* and excludes *a systemic reaction that involves the injection site e.g., generalised urticaria* [22].

Ethics

BRIT is a research database and holds both identifiable and non-identifiable participant data. All participants complete written consent to join the registry. Patient identifiable data is shared with the registry only with informed written consent. These identifiers are used to enable the local consultant users and their healthcare team to identify the participant. Identifiers are not shared outside of the local clinical team and are not analysed with the central registry. Anonymous analysis of registry data is limited to the stated objectives of the registry. Applications to NHS R&D offices through Integrated Research Application System (IRAS) are not required.

Healthcare users are not research sites for the purposes of the Research Governance Framework (RGF). Individual allergy services are expected to have conducted a management review in the process of establishing the registry at their local centre in terms of its feasibility, impact on standards of care and sustainability as an addition to current service provision. Allergy services must strictly adhere to the data protection best practice.

Ethics approval is required for analysis of research hypotheses using registry data. The BRIT Steering committee plan to submit an application for Research Ethics Committee approval for this purpose as part of the first phase of registry development by the end of 2021.

Data protection

BRIT is held on secure servers within the NHS. The Registry is managed by Dendrite Clinical Systems Ltd, who have many years of experience in hosting similar national and international clinical registries. BRIT contains both identifiable and non-identifiable participant data. All participants (or participants' parent/legal guardian) must have signed informed consent before their data can be entered onto the Registry.

1. Each participant is identified by a unique code number. This is a randomly generated number and is not pseudo-anonymous.
2. Gender, gender alignment, ethnicity and the postcode are available for analysis, but only with the participant's express consent to share this information.
3. Personal data of participants are available to those directly involved in their care. It is not available in registry data downloads used for analysis.
4. The participant's name, DOB and e-mail contact information are stored on the registry, but can only accessed by the participant or their consultant or delegated user.
5. Dates of birth are converted to age before download.

The Registry Steering Committee (RSC) oversees the running of the registry. The data are owned by BSACI and not the NHS, nor the funders nor the web-host. The RSC is made up of BSACI members and has patient group representatives from the Anaphylaxis Campaign and Allergy UK. The RSC is independent of the funders and reports directly to the BSACI Council.

The RSC does not have access to individual participant identifiable information, but can use the non-identifiable data for analysis in line with the aims and objectives of the Registry.

The RSC will also review applications to use registry data for research purposes from organisations outside of BSACI, but this will be confined to non-identifiable data and will not be commercially sensitive in nature.

A note on the conventions used throughout this report

There are several conventions used in the report in an attempt to ensure that the data are presented in a simple and consistent way. These conventions relate largely to the tables and the graphs, and some of these conventions are outlined below.

The specifics of the data used in any particular analysis are made clear in the accompanying text, table or chart. For example, many analyses sub-divide the data on the basis of the type of immunotherapy, and the titles for both tables and charts will reflect this fact.

Conventions used in tables

On the whole, unless otherwise stated, the tables and charts in this report record the number of procedures (see the example below).

Venom immunotherapy: age & gender

		Gender			
		Female	Male	Unspecified	All
Age at consent	<10	2	3	0	**5**
	10-19	3	9	0	**12**
	20-29	2	2	0	**4**
	30-39	0	1	0	**1**
	40-49	8	3	0	**11**
	50-59	11	13	0	**24**
	60-68	20	15	0	**35**
	>69	5	6	0	**11**
	Unspecified	0	0	0	**0**
	All	**51**	**52**	**0**	**103**

Each table has a short title that is intended to provide information on the subset from which the data have been drawn, such as the patient's gender or particular patient sub-grouping under examination.

The numbers in each table are colour-coded so that entries with complete data for all of the components under consideration (in this example both age and gender) are shown in regular black text. If one or more of the database questions under analysis is blank, the data are reported as unspecified in red text. The totals for both rows and columns are highlighted as **emboldened** text.

Some tables record percentage values; in such cases this is made clear by the use of an appropriate title within the table and a % symbol after the numeric value.

Rows and columns within tables have been ordered so that they are either in ascending order (age at procedure: <20, 20-24, 25-29,30-34, 35-39 years, *etc.*; post-procedure stay 0, 1, 2, 3, >3 days; *etc.*) or with negative response options first (No; None) followed by positive response options (Yes; One, Two, *etc.*).

Row and column titles are as detailed as possible within the confines of the space available on the page. Where a title in either a row or a column is not as detailed as the authors would have liked, then footnotes have been added to provide clarification.

There are some charts in the report that are not accompanied by data in a tabular format. In such cases the tables are omitted for one of a number of reasons:

- insufficient space on the page to accommodate both the table and graph.
- there would be more rows and / or columns of data than could reasonably be accommodated on the page (for example, Kaplan-Meier curves).
- the tabular data had already been presented elsewhere in the report.

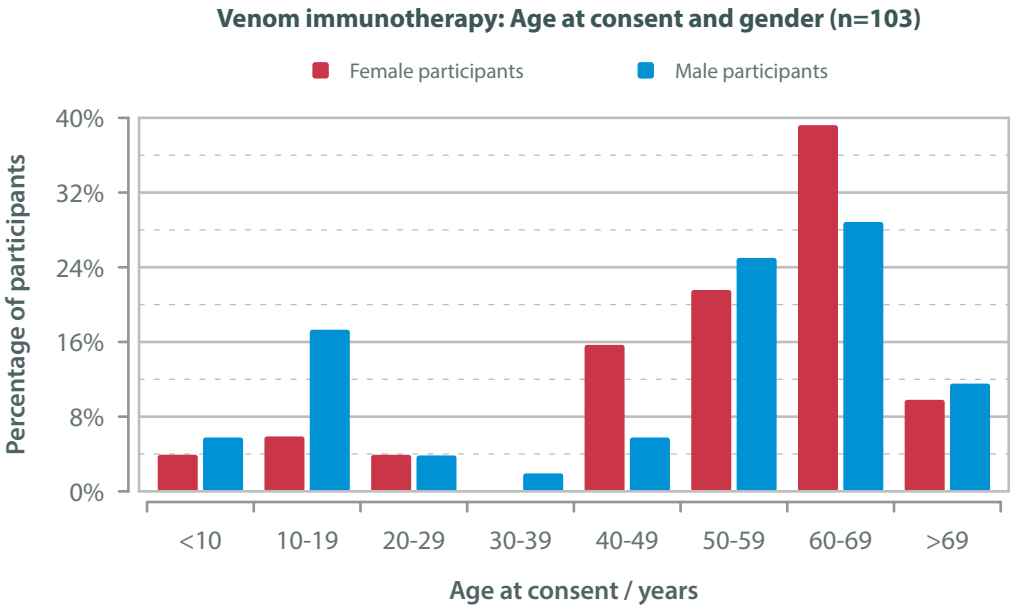
Conventions used in graphs

The basic principles applied when preparing graphs for this First Registry for Immunotherapy Report were based, as far as possible, upon William S Cleveland's book *The elements of graphing data* [1]. This book details both best practice and the theoretical bases that underlie these practices, demonstrating that there are sound, scientific reasons for plotting charts in particular ways.

Counts: The counts (shown in parentheses at the end of each graph's title as n=) associated with each graph can be affected by a number of independent factors and will therefore vary from chapter to chapter and from page to page. Most obviously, many of the charts in this report are graphic representations of results for a particular group (or subset) extracted from the database, such as patients having venom immunotherapy. This clearly restricts the total number of database-entries available for any such analysis.

In addition to this, some entries within the group under consideration have data missing in one or more of the database questions under examination (reported as unspecified in the tables); all entries with missing data are excluded from the analysis used to generate the graph because they do not add any useful information.

For example, in the graph below, only the database entries where the patient is having venom immunotherapy and both the patient's age and gender are known are included in the analysis; this comes to 103 patient-entries (any entries with unspecified data would have been excluded from the chart).



Confidence interval: In the charts prepared for this report, most of the bars plotted around rates (percentage values) represent 95% confidence intervals [2]. The width of the confidence interval provides some idea of how certain we can be about the calculated rate of an event or occurrence. If the intervals around two rates do not overlap, then we can say, with the specified level of confidence, that these rates are different; however, if the bars do overlap, we cannot make such an assertion.

Bars around averaged values (such as patients' age, post-operative length-of-stay, *etc.*) are classical standard error bars or 95% confidence intervals; they give some idea of the spread of the data around the calculated average. In some analyses that employ these error bars there may be insufficient data to legitimately calculate the standard error around the average for each sub-group under analysis; rather than entirely exclude these low-volume sub-groups from the chart their arithmetic average would be plotted without error bars. Such averages without error bars are valid in the sense that they truly represent the data submitted; however, they should not to be taken as definitive and therefore it is recommended that such values are viewed with extra caution.

1. Cleveland WS. *The elements of graphing data*. 1985, 1994. Hobart Press, Summit, New Jersey, USA.
2. Wilson EB. Probable inference, the law of succession, and statistical inference. *Journal of American Statistical Association*. 1927; **22**: 209-212.

Database overview

Registered users

The table below shows the registered speciality of the primary consultant users of the registry. They were practising at 65 separate hospitals in the United Kingdom.

Registered users of the BSACI Registry for Immunotherapy (BRIT)

Class of user			Count	Percentage
	Owner's specialty	Allergy	20	19.8%
		Immunology	11	10.9%
		Paediatrics	32	31.7%
		Paediatric AI & ID[i]	20	19.8%
		General Practice	2	2.0%
		Other adult speciality	6	5.9%
		Other paediatric specialty	2	2.0%
		Nurse consultant	2	2.0%
		Unspecified	6	5.9%
		All	**101**	
	Delegate	Consultant level doctor / HCP[ii]	7	9.2%
		Non consultant level doctor	8	10.5%
		Nurse Specialists	36	47.4%
		Admin	1	1.3%
		Unspecified	24	31.6%
		All	**76**	

Participants

The charts on the following page show the growth in participants to the registry since its launch. They do not suggest that there is an increase in the number of patients treated nationally, but do show that more of the current cohort is participating in the project.

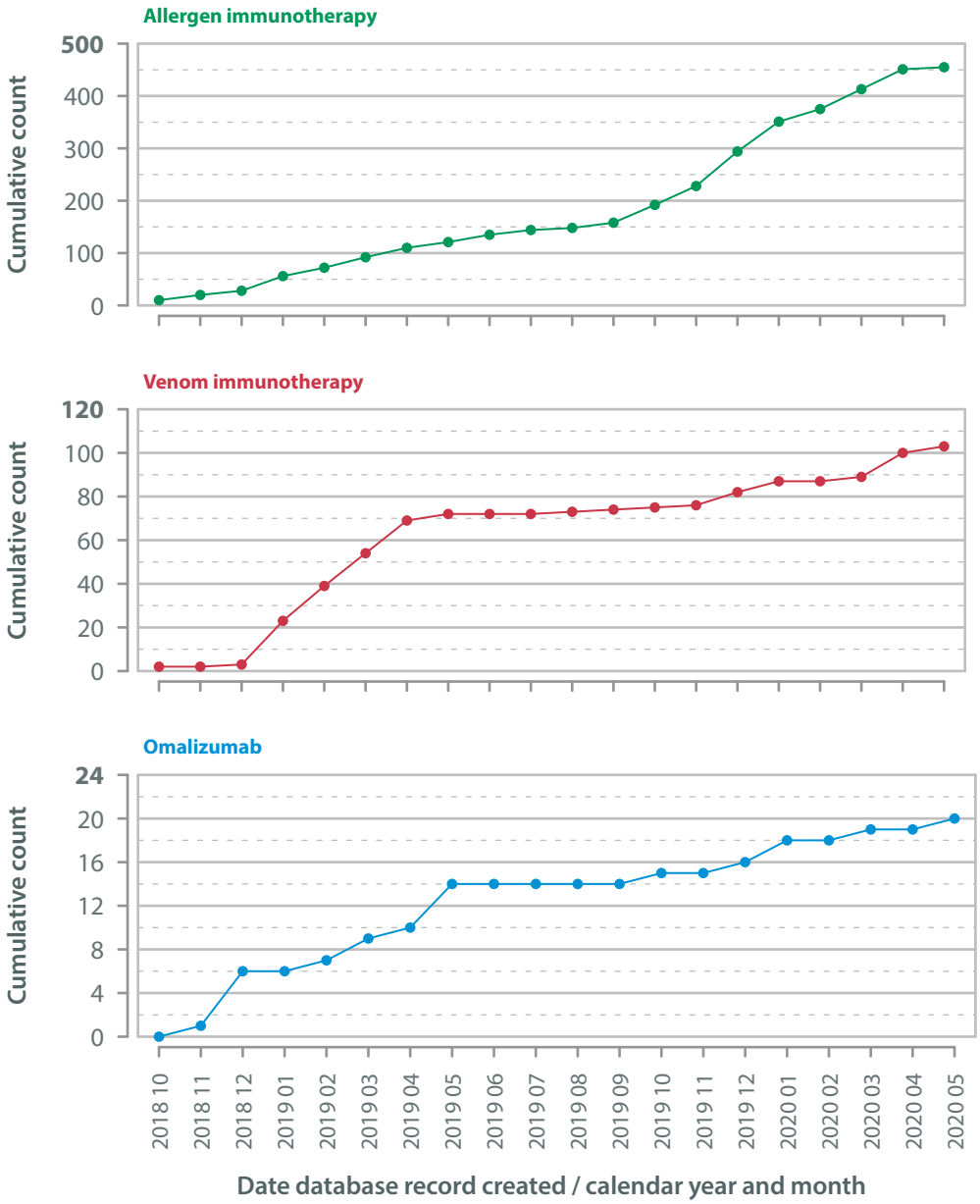
i. AI & ID: Allergy Immunology & Infectious Diseases

ii. HCP: Healthcare Professional, *e.g.*, Nurse Consultant.

Type of immunotherapy

		Count	Percentage
Type of immunotherapy	Allergen	455	78.7%
	Venom	103	17.8%
	Omalizumab	20	3.5%
	Unspecified	2	
	All	**580**	

The growth of the database in terms of participants



Access to specialist services

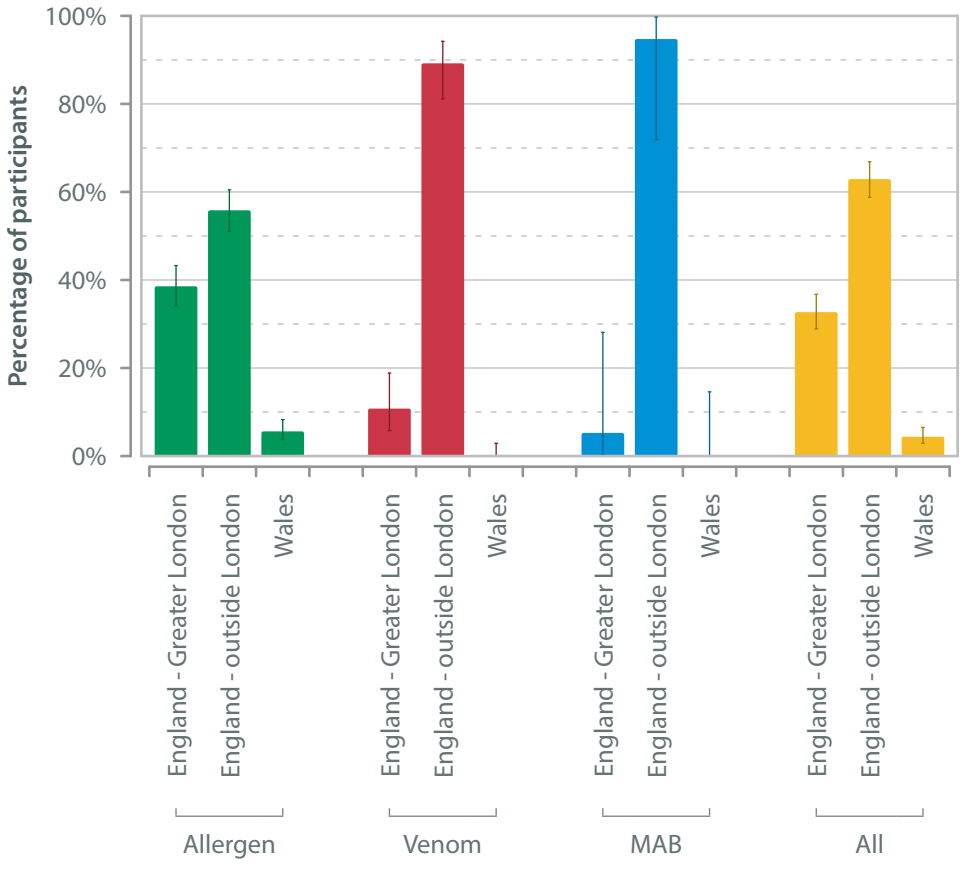
Location of participants

Most engagement with the registry has occurred in England outside of London with signs of early engagement from the large clinics in London. There were no recorded participants in Scotland or Northern Ireland.

The participant's country of residence

		Type of immunotherapy				
		Allergen	Venom	Omalizumab	Unspecified	All
Country of residence	England - Greater London	172	11	1	2	**186**
	England - outside London	249	91	18	0	**358**
	Wales	25	0	0	0	**25**
	Unspecified	9	1	1	0	**11**
	All	**455**	**103**	**20**	**2**	580

Location of the participants



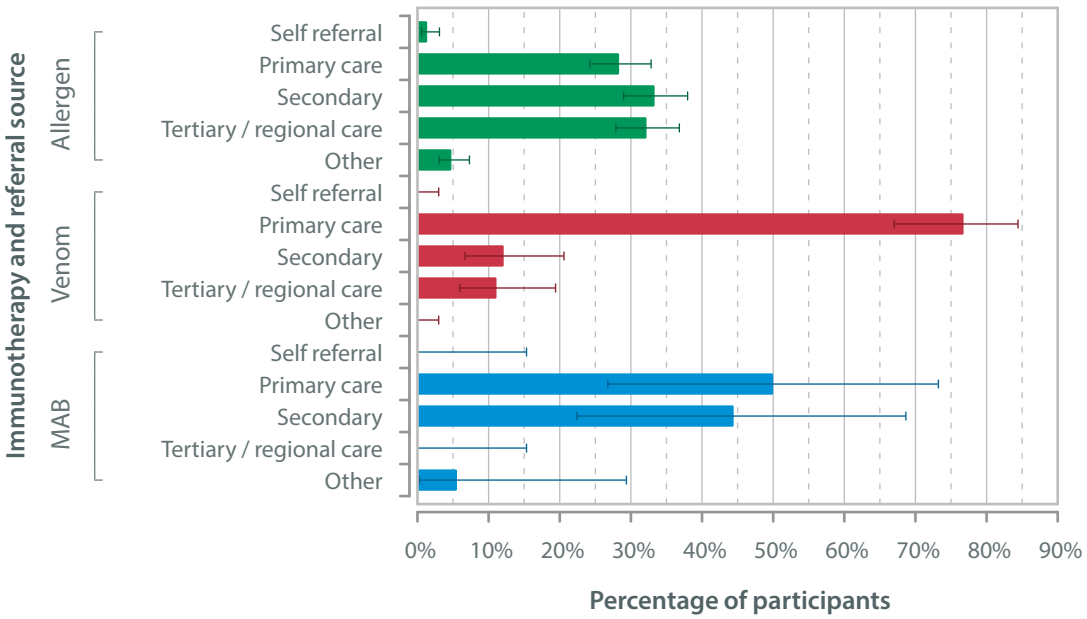
Type of immunotherapy and country of residence

Referral source

Referral source

Referral source	Type of immunotherapy				
	Allergen	Venom	Omalizumab	Unspecified	All
Self referral	6	0	0	0	**6**
Primary care	125	76	9	0	**210**
Secondary care	147	12	8	0	**167**
Tertiary / regional care	142	11	0	0	**153**
Other	21	0	1	0	**22**
Unspecified	14	4	2	2	**22**
All	**455**	**103**	**20**	**2**	580

Referral sources according to the participant's type of immunotherapy

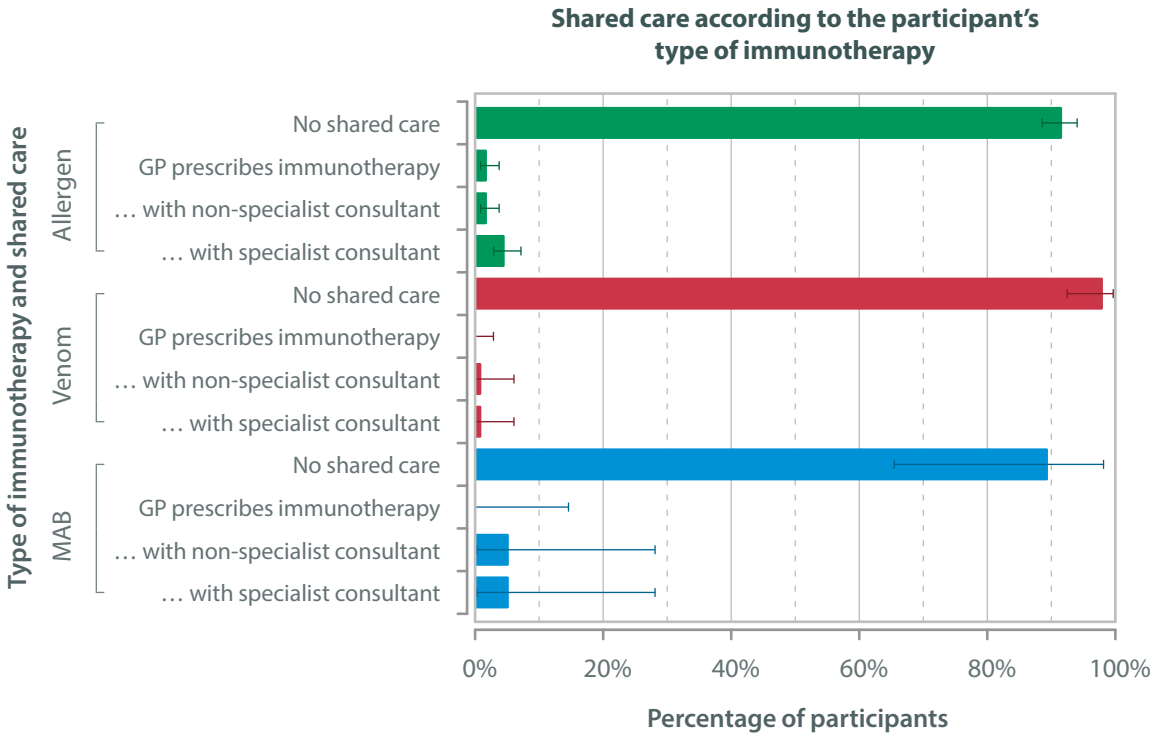


Shared care

Occasionally allergy centres may need to share care with another practice; this is because regional immunotherapy centres may cover large geographical areas where it is not always practical for patients to travel for care. Injection immunotherapy such as SCIT, VIT and OMA should only be shared with secondary care hospital-based practice, whilst sublingual immunotherapy can be shared with both primary and secondary care.

Shared care from another practice

		Type of immunotherapy			
		Allergen	Venom	Omalizumab	Unspecified
Any shared care	No shared care	397	101	17	0
	GP prescribes immunotherapy	8	0	0	0
	… with non-specialist consultant	8	1	1	0
	… with specialist consultant	20	1	1	0
	Unspecified	22	0	1	2
	All	**455**	**103**	**20**	**2**



Consent for PROMs

Written consent is mandatory before a participant is included in the registry. This is because the registry includes personal identifiers to help clinicians identify their patients in the registry. The consent sought here is for inclusion in the email reporting programme of the registry. Active participants are sent emails with links to complete on-line PROM forms. Participants can continue to be part of the reporting scheme after they have finished active treatment; in this way the registry can collect long-term outcome data on immunotherapy. The email reporting is popular and most participants choose to be part of the scheme.

Consent given by participants or their parents / legal guardians for inclusion in the BRIT e-mail PROM programme

		Consent given for participation in e-mail PROM programme			
		No	Yes	Unspecified	Consent rate
Type of immunotherapy	Allergen	15	431	9	96.6%
	Venom	8	94	1	92.2%
	Omalizumab	0	19	1	100.0%
	Unspecified	0	2	0	100.0%
	All	**23**	**546**	**11**	**96.0%**

Allergen immunotherapy

Age and gender

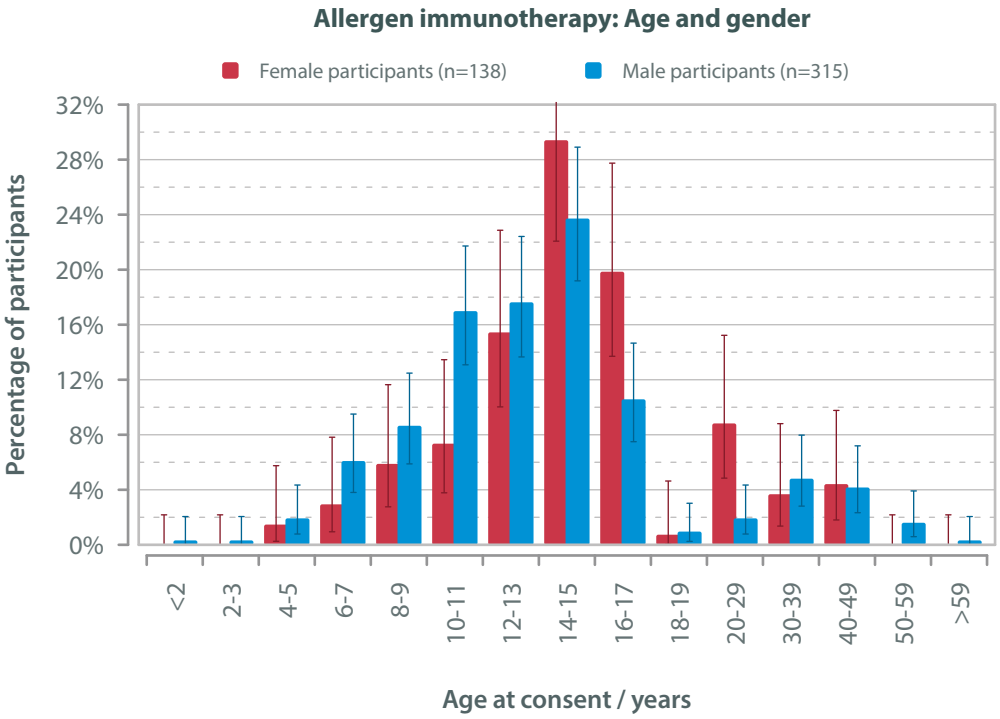
The majority of allergen immunotherapy (AIT) participants were children with only 16% (73/455) over the age of 16 years. There is a slight male predominance (OR 2.28), which is in keeping with known trends for allergic disease in this age group.

Allergen immunotherapy: age and gender of the participants at the time of consent

Age at consent / years	Gender: Female	Male	Unspecified	All
<2	0	1	0	**1**
2-3	0	1	0	**1**
4-5	2	6	0	**8**
6-7	4	19	0	**23**
8-9	8	27	0	**35**
10-11	10	53	0	**63**
12-13	21	55	1	**77**
14-15	40	74	0	**114**
16-17	27	33	0	**60**
18-19	1	3	0	**4**
20-29	12	6	0	**18**
30-39	5	15	0	**20**
40-49	6	13	0	**19**
50-59	0	5	0	**5**
60-69	0	1	0	**1**
Unspecified	2	3	1	**6**
All	**138**	**315**	**2**	**455**

Allergen immunotherapy: basic age statistics for male & female participants

		Age statistics: Count	Median (IQR)	Average (95% CI)
Gender	Female	138	**15.0** (12.0-17.0)	**17.8** (15.6-19.9)
	Male	315	**13.0** (10.0-16.0)	**16.4** (15.0-17.9)
	All	**455**	**14.0** (11.0-16.0)	**17.0** (15.8-18.2)


Allergen immunotherapy: Age and gender
Female participants (n=138)
Male participants (n=315)
Percentage of participants
32%
28%
24%
20%
16%
12%
8%
4%
0%
<2
2-3
4-5
6-7
8-9
10-11
12-13
14-15
16-17
18-19
20-29
30-39
40-49
50-59
>59
Age at consent / years

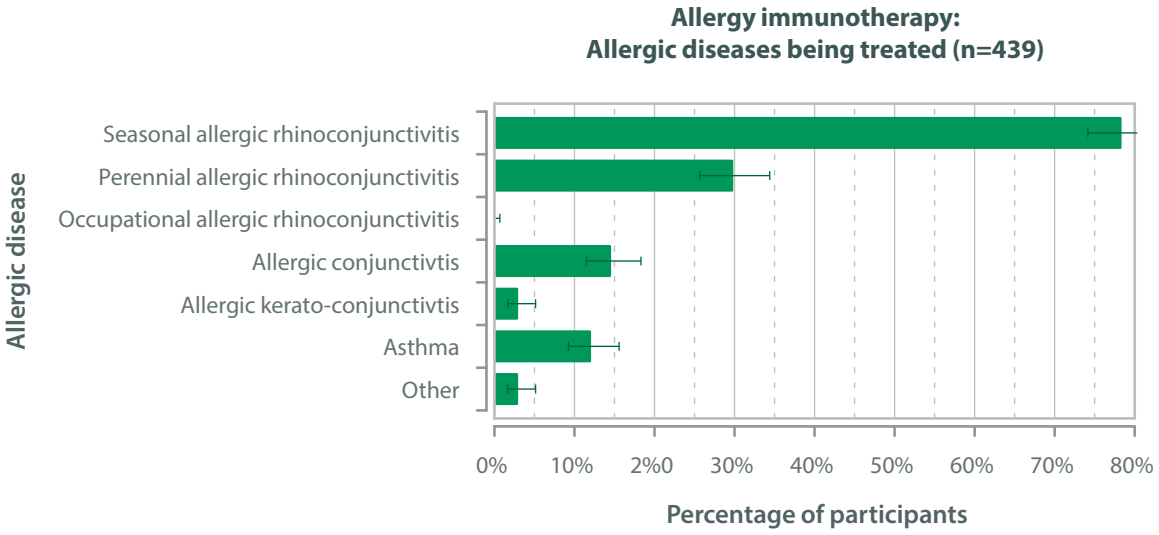
Participants' allergies

Allergic diseases being treated

Three-quarters of participants had seasonal allergic rhinitis and one-third perennial symptoms. In keeping with current national asthma guidelines, where allergen immunotherapy is not recommended, only a minority were treated to help with asthma control.

Allergen immunotherapy: allergic diseases being treated

Allergic diseases	Incidence			
	No	Yes	Unspecified	Rate
Seasonal allergic rhinoconjunctivitis	95	344	16	78.4%
Perennial allergic rhinoconjunctivitis	308	131	16	29.8%
Occupational allergic rhinoconjunctivitis	439	0	16	0.0%
Allergic conjunctivtis	375	64	16	14.6%
Allergic kerato-conjunctivtis	426	13	16	3.0%
Asthma	386	53	16	12.1%
Other	426	13	16	3.0%

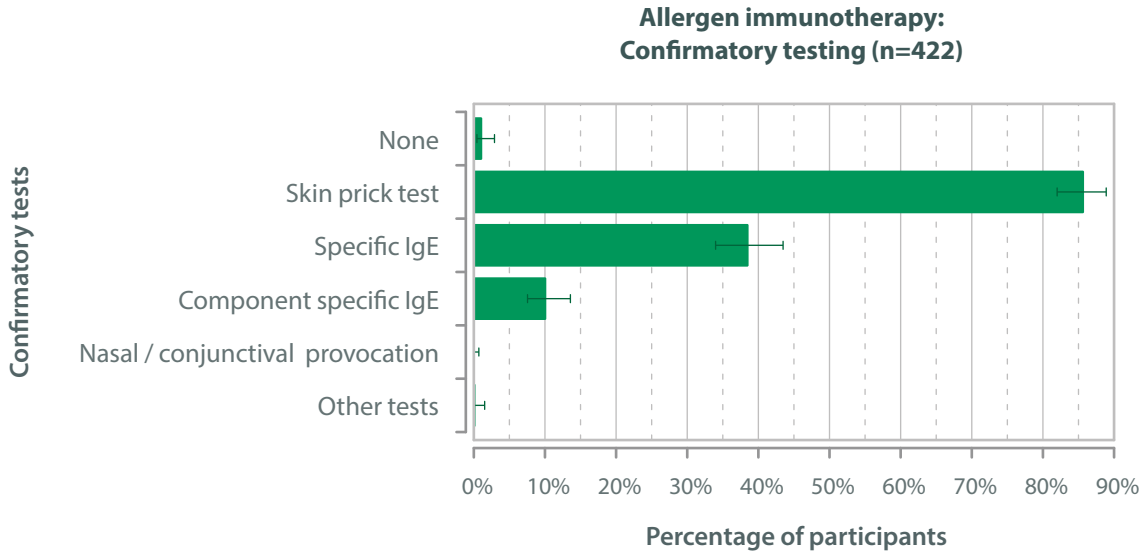


Confirmatory testing

Current guidelines recommend allergy testing before starting allergen immunotherapy. It is reassuring that 98.8% of participants had allergy testing before starting treatment.

Allergen immunotherapy: confirmatory testing

		Count	Percentage
Confirmatory testing	No confirmatory testing	5	1.2%
	Skin prick test	362	85.8%
	Specific IgE	163	38.6%
	Component specific IgE	43	10.2%
	Nasal / conjunctival provocation	0	0.0%
	Other	1	0.2%
	Unspecified	33	
	Participants	**455**	



Persistent symptomatic allergic rhinitis

Immunotherapy is reserved for those who have failed conventional treatment. 96.5% of participants were in this group. These rules do not apply in private practice where less severe disease may be treated on request.

Allergen immunotherapy: persistent symptoms of allergic rhinitis despite intranasal steroids and antihistamines taken regularly

		Count	Percentage
Persistent symptomatic allergic rhinitis	No	15	3.5%
	Yes	408	96.5%
	Unspecified	32	
	All	**455**	

Treatments

Total number of courses per participant

In its current format these data describe two different elements and will require further analysis. For some participants it reflects the number of seasonal treatments of the same allergen immunotherapy *e.g.,* grass sub-lingual immunotherapy (SLIT) season 1, in 2018, season 2 in 2019 and season 3 in 2020, would be described here as 3 courses of treatment. For others it records treatments with different allergen immunotherapy regimes *e.g.,* SLIT grass alone in 2018 then stopped, SLIT grass and tree in 2019, which then continues from 2019 to the current date (2020 at the time data were sampled for the report), recorded here as 2 courses of treatment. The registry was designed so that no further adjustment is required once a course of allergen immunotherapy has been started until it is finally stopped, often several years later. It is not necessary to record the treatment as *stopped* after each summer season, the registry assumes ongoing pre- or co-seasonal treatment until a stop date is entered, when the full course of treatment has been completed.

Allergen immunotherapy: recorded courses of treatment

		Count	Percentage of participants
Total number of courses	0	83	18.2%
	1	252	55.4%
	2	100	22.0%
	3	18	4.0%
	>3	2	0.4%
	All	**455**	

Current status of treatment

Allergen immunotherapy: current status of immunotherapy treatment for each participant

		Number of courses stopped				
		0	**1**	**2**	**>2**	**All**
Number of courses starting	0	83	8	2	0	**93**
	1	244	25	1	2	**272**
	2	73	2	0	0	**75**
	3	15	0	0	0	**15**
	All	**415**	**35**	**3**	**2**	**455**

Treatment status and route

The number of treatment courses started and stopped is compared for each course of treatment between subcutaneous immunotherapy (SCIT) and sub-lingual immunotherapy (SLIT) routes of allergen immunotherapy.

Allergen immunotherapy: status and route of each recorded course of treatment

			Count	Percentage per timing
Status & route of immunotherapy	Starting	Subcutaneous	176	37.8%
		Sub-lingual	289	62.2%
		Unspecified	2	
	Stopped	Subcutaneous	17	34.0%
		Sub-lingual	33	66.0%
		Unspecified	0	
	Unspecified	Subcutaneous	4	21.1%
		Sub-lingual	15	78.9%
		Unspecified	41	

Allergen and route of treatment

Most participants were treated with SCIT or SLIT using grass or tree pollen extracts, to help with their seasonal allergic symptoms. There was a predominance of house dust mite allergen immunotherapy by the SLIT route rather than SCIT. A quarter (26%, 112/422) of participants received more than one allergen.

Allergen immunotherapy: allergen and route of administration

		Route			
		Subcutaneous	Sub-lingual	Unspecified	Percentage sub-lingual
Allergen	Grass	159	156	0	49.5%
	Tree	50	105	0	67.7%
	House dust mite	13	79	0	85.9%
	Cat	0	2	0	100.0%
	Dog	0	1	0	100.0%
	Unspecified	6	15	43	
	Count of courses	**197**	**337**	**43**	

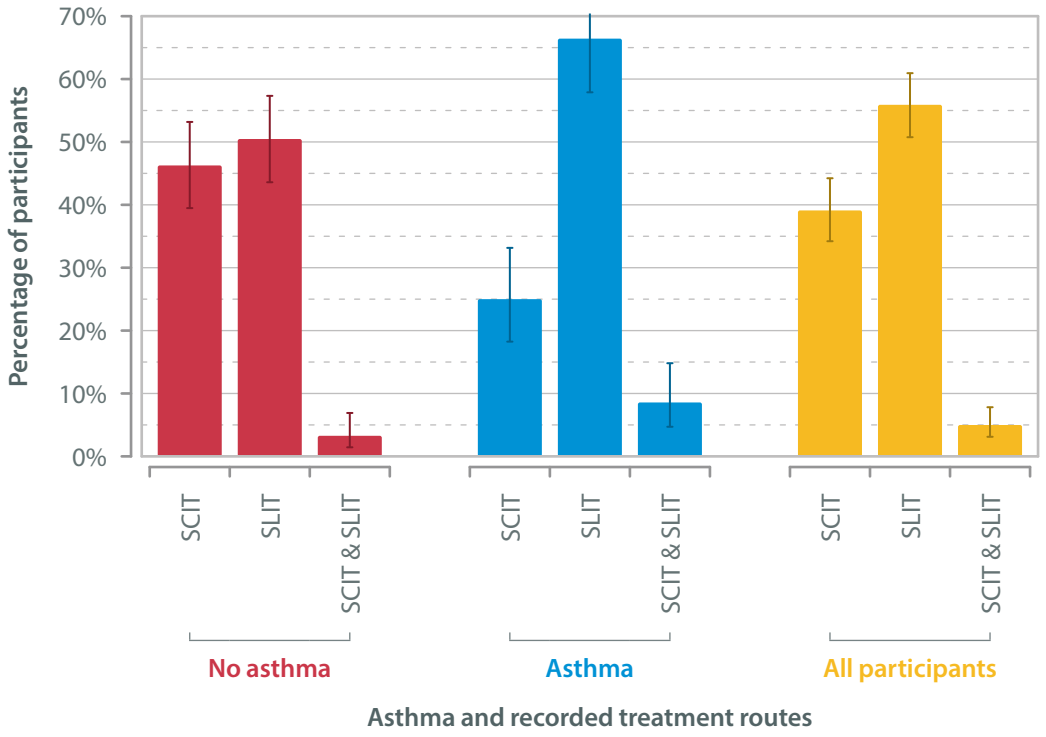
Asthma and route of allergen immunotherapy

Asthma is a relative contraindication to allergen immunotherapy. The table shows that 46% sub-lingual immunotherapy (SLIT) and 26% of subcutaneous immunotherapy (SCIT) participants had asthma.

Allergen immunotherapy: asthma and recorded immunotherapy treatment routes

		Treatment routes recorded				
		SCIT	SLIT	SCIT & SLIT	Unspecified	All
Asthma	No	99	108	7	47	**261**
	Yes	35	93	12	20	**160**
	Unspecified	15	12	0	7	**34**
	All	**149**	**213**	**19**	**74**	**455**

Allergen immunotherapy:
Diagnosis of asthma and the route of immunotherapy



Asthma severity in allergen immunotherapy

The majority of asthma treatment was towards the mild end of disease with either no preventer or low-dose inhaled corticosteroid (ICS), alone or in combination with other agents. High-dose ICS or steroids or other immunosupression was recorded, but only in a minority of the participants with asthma.

Allergen immunotherapy: the severity of asthma; patients with asthma recorded

		Counts	Percentages
Severity of asthma by current preventer therapy	No preventer required	37	23.4%
	Inhaled corticosteroid (low dose)	96	60.8%
	Leukotriene antagonist	38	24.1%
	Long acting beta agonist (LABA)	38	24.1%
	Inhaled corticosteroid (high dose)	9	5.7%
	Continuous or frequent oral steroids	1	0.6%
	Monoclonal antibody therapy	1	0.6%
	Unspecified	2	
	Patient denominator	**160**	

Matching of clinical sensitivity to allergens in immunotherapy

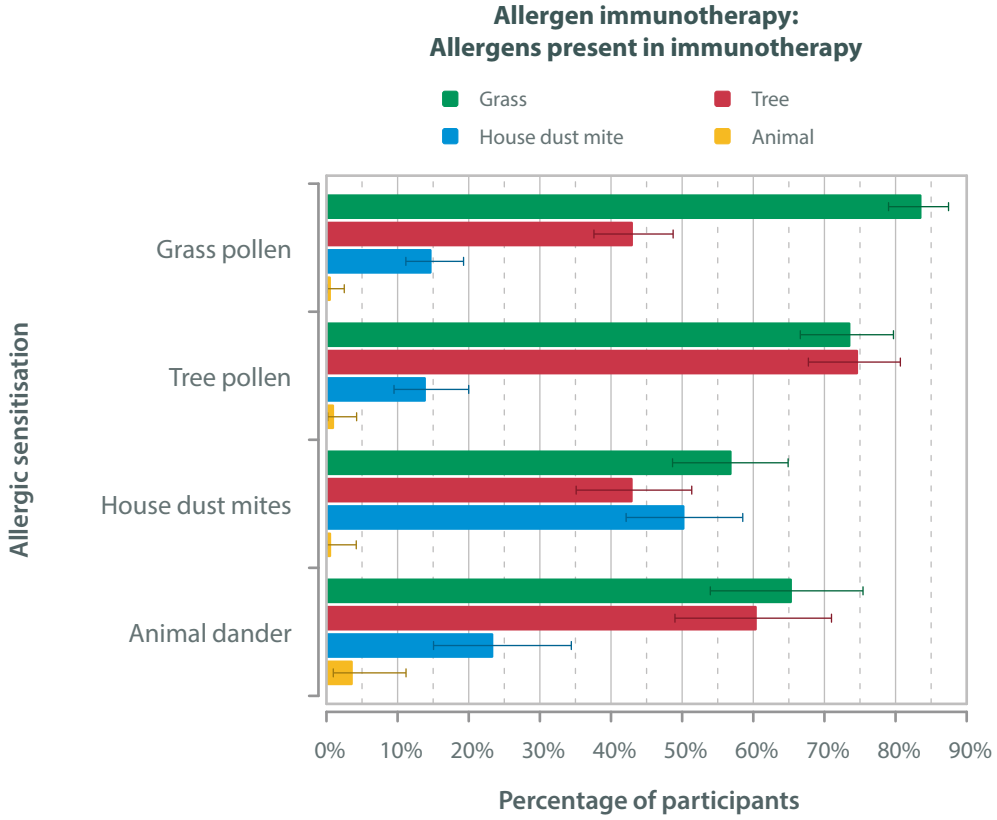
For effective treatment it is essential that the individual is sensitised to the allergens being used in treatment. Close matching of clinical sensitivity of the individual to the allergens present in the immunotherapy product is required for a good outcome.

This table and graph have summarised treatment matching in the registry. For example, the table shows that 378 participants were allergic to grass of whom, 266 had grass allergen in their treatment. As shown in the graph this is 83% (266/(378-60)) of grass-pollen-allergic participants who have grass pollen in their treatment.

Many participants are poly-sensitised but do not receive treatment for all identified allergens. For example, only 3 of 87 (3.7%) of the animal-dander-allergic participants received animal dander as part of their immunotherapy regime.

Allergen immunotherapy: participant's allergy and allergens in immunotherapy

		Allergens present in treatment					
		Grass	Tree	House dust mite	Animal	Unspecified	Participants
Sensitisation	Grass	266	137	47	2	60	**378**
	Tree	137	139	26	2	18	**204**
	House dust mite	86	65	76	1	28	**179**
	Animal	53	49	19	3	6	**87**



Reasons for stopping treatment

Of the 50 cases that had stopped allergen immunotherapy at the time of analysis only 9 reported that this was for a reason other than the completion of the treatment course. Four were related to poor adherence (SLIT) and 5 for side effects. The adverse events associated with allergen immunotherapy are recorded below.

Allergen immunotherapy: reasons for stopping courses of treatment

		Occurrences				
		No	Yes	Unspecified	Treatments	Rate
Reasons for stopping IT	Poor adherence	43	4	3	50	8.5%
	Side effects	42	5	3	50	10.6%
	New diagnosis of asthma	47	0	3	50	0.0%
	Adverse events	44	4	2	50	8.3%

Adverse events

The incidence of adverse events

There were 20 recorded adverse events in participants receiving allergen immunotherapy this gives an overall rate of 4.4%. More events were reported in those receiving both subcutaneous immunotherapy (SCIT) and sub-lingual immunotherapy (SLIT) at the same time.

Allergen immunotherapy: adverse events and the route of immunotherapy

		Route(s) of immunotherapy				
		SCIT	SLIT	SCIT & SLIT	Unspecified	All
Any adverse events recorded	None recorded	142	204	17	72	**435**
	One or more recorded	7	9	2	2	**20**
	All	149	213	19	74	**455**
	Adverse event rate	4.7%	4.2%	10.5%	2.7%	**4.4%**

Type of adverse event

There was a split between local injection site (SCIT) or oral symptoms (SLIT) reported and more generalised allergic reactions. There was one case of anaphylaxis reported. For most patients with adverse events the reactions were relatively mild and did not require dose adjustment. One-quarter of reported adverse events resulted in immunotherapy being stopped. Most reactions occurred either on first dose or during up-dosing. Some adverse reactions occurred hours and even, in some cases, days after administration of the allergen therapy, these would not relate to immediate allergic reactions or anaphylaxis, which tend to occur promptly.

Allergen immunotherapy: type of adverse events

		Route(s) of immunotherapy				
		SCIT	SLIT	SCIT & SLIT	Unspecified	All
Type of adverse events	Injection site symptoms	5	0	0	1	**6**
	Oral symptoms	2	7	0	1	**10**
	Suspected anaphylaxis	1	0	0	0	**1**
	Systemic adverse reaction	7	5	2	0	**14**
	Total adverse reactions	**15**	**12**	**2**	**2**	**31**

Details of allergen immunotherapy adverse events

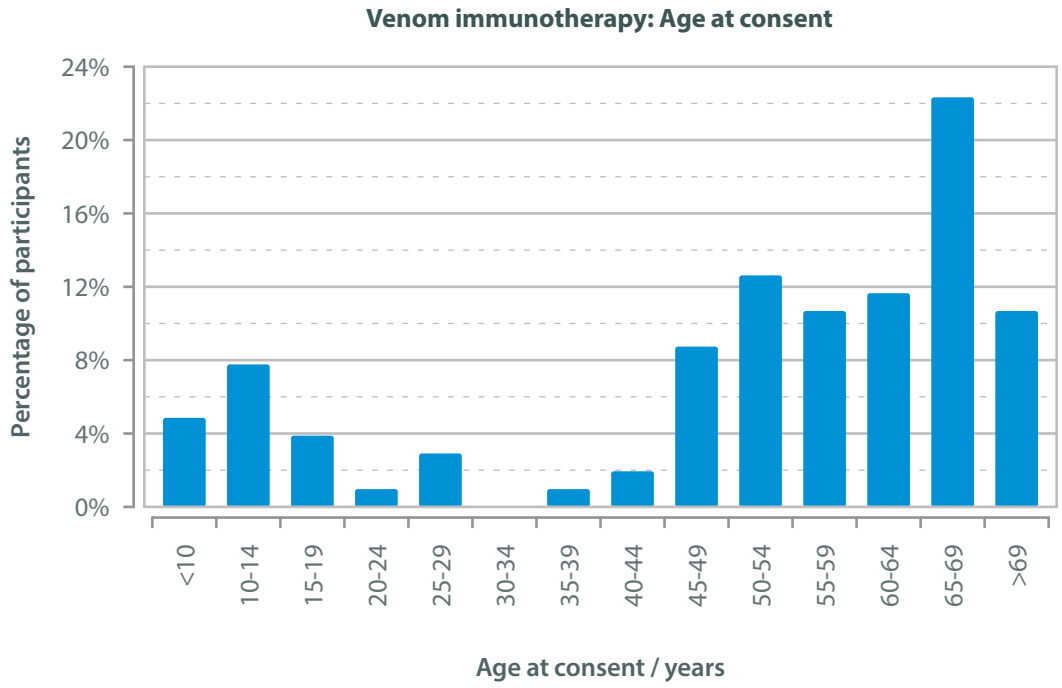
		Count	Percentage
Change in immunotherapy because of the adverse event	No change in dose	14	45.2%
	Reduction < 50% in dose for next administration	4	12.9%
	Same dose repeated	4	12.9%
	Started from initial dose again	1	3.2%
	Stopped immunotherapy	8	25.8%
When did the adverse event happen	First dose	8	25.8%
	Maintenance	8	25.8%
	Up-dosing	14	45.2%
	Not applicable	1	3.2%
Onset of the adverse event	Immediate	2	6.7%
	Under 30 minutes	4	13.3%
	Over 30 minutes	7	23.3%
	Hours	12	40.0%
	Days	5	16.7%
Adverse event related to immunotherapy	Related	26	86.7%
	Unrelated	4	13.3%
	Unspecified	1	

Venom immunotherapy

Venom immunotherapy is indicated for the treatment of systemic allergic reactions to bee and wasp stings in adults and children.

Age at consent

Venom immunotherapy shows a bimodal age distribution peaking in older children and younger teenagers (10-14 years) and again in older adults (65 -69). In clinical practice VIT is more common in adults than in children.



Indication

Current venom immunotherapy guidelines restrict its use to the indication categories recorded by the registry, in the presence of detectable IgE to venom. Most venom immunotherapy participants have suffered a severe reaction to a sting.

More people receive wasp venom immunotherapy as opposed bee venom immunotherapy. Conventional weekly up-dosing is the norm. Most participants are undergoing active treatment on their first course of venom immunotherapy. We expect to see this change as participants move from Pharmalgen, which was withdrawn in late 2019, to Alutard SQ and other products. There is little data on this change-over process in the registry at present.

Venom immunotherapy: indication for venom immunotherapy

		Count	Percentage
Indication	Severe systemic reaction to a sting	54	58.1%
	Moderate severity systemic reaction to a sting	36	38.7%
	Mild reaction to sting but with raised baseline tryptase	0	0.0%
	Mild reaction to sting but with high likelihood of future stings	2	2.2%
	Mild reaction to sting but with adverse effect on quality-of-life	1	1.1%
	Unspecified	10	
	All	**103**	

Treatments

Total number of courses per participant

The registry records the date of the first injection. After that it assumes up-dosing and ongoing maintenance until the last dose is entered and the treatment course has stopped. The method of up-dosing is recorded *e.g.*, weekly (conventional), rush, and ultra-rush. The user does not need to record each subsequent injection. Changes to type of venom immunotherapy , such as switch over from one brand to another counts as more than one course. Brand A is stopped on the day of last injection and Brand B started on the day of first injection.

Venom immunotherapy: recorded courses of treatment

		Count	Percentage of participants
Total number of courses	0	20	19.4%
	1	79	76.7%
	2	4	3.9%
	All	**103**	

Current status of treatment

Venom immunotherapy: current status of immunotherapy treatment for each participant

		Number of courses stopped			
		0	**1**	**2**	**All**
Number of courses starting	0	20	0	0	**20**
	1	77	2	0	**79**
	2	1	2	1	**4**
	All	**98**	**4**	**1**	**103**

Immunotherapy choice

Treatment for wasp venom allergy is more common than for bee venom allergy.

Venom immunotherapy: immunotherapy choice

		Count	Percentage
Immunotherapy choice	Bee	27	31.0%
	Wasp	60	69.0%
	Unspecified	5	
	Courses	**92**	

Induction

Venom immunotherapy is commenced at low doses of venom and is gradually increased as tolerated until a maintenance dose is achieved, normally the equivalent of a full sting. Current BSACI guidelines offer a range of options for up-dosing as indicated in the table [i]. The majority of participants receive conventional up-dosing with weekly injections over 8-12 weeks. When switching between products during the maintenance phase the dose may be reduced or split between two injections [23]. Only aqueous products should be used for rush and ultra-rush protocols [24].

Venom immunotherapy: induction

		Count	Percentage
Type of induction	Continued maintenance - no dose adjustment	1	1.8%
	Continued maintenance - first dose split over 30 minutes [i]	2	3.5%
	Conventional up-dosing (over 3-4 months)	51	89.5%
	Weekly up-dosing over 15 weeks (Alutard)	2	3.5%
	Weekly up-dosing over 25 weeks (Alutard)	0	0.0%
	Cluster up-dosing over 7 weeks (Alutard)	0	0.0%
	Rush up-dosing (over 1-3 weeks) [ii]	0	0.0%
	Ultra rush up-dosing (over 2-3 days) [ii]	1	1.8%
	Unspecified	35	
	All courses	**92**	

Reasons for stopping treatment

Six participants stopped venom immunotherapy to date. All were due to completion of course or withdrawal of current product. There were three adverse events as outlined below.

Venom immunotherapy: reasons for stopping courses of treatment

		Occurrences				
		No	Yes	Unspecified	Treatments	Rate
Reasons for stopping IT	Poor adherence	6	0	0	6	0.0%
	Side effects	6	0	0	6	0.0%
	New diagnosis of asthma	6	0	0	6	0.0%
	Adverse events	6	0	0	6	0.0%

Adverse events

3 adverse events reported in total for two participants; all three were systemic.

One resulted in a >50% reduction in dose; the other two (same patient) resulted in no change.

The first was at the time of up-dosing and the other two during maintenance.

The first was under 30 minutes after the last immunotherapy dose; the other two over 30 minutes afterwards.

The first participant's reaction was *expected*; the other participant had one *expected* and one *unexpected* event.

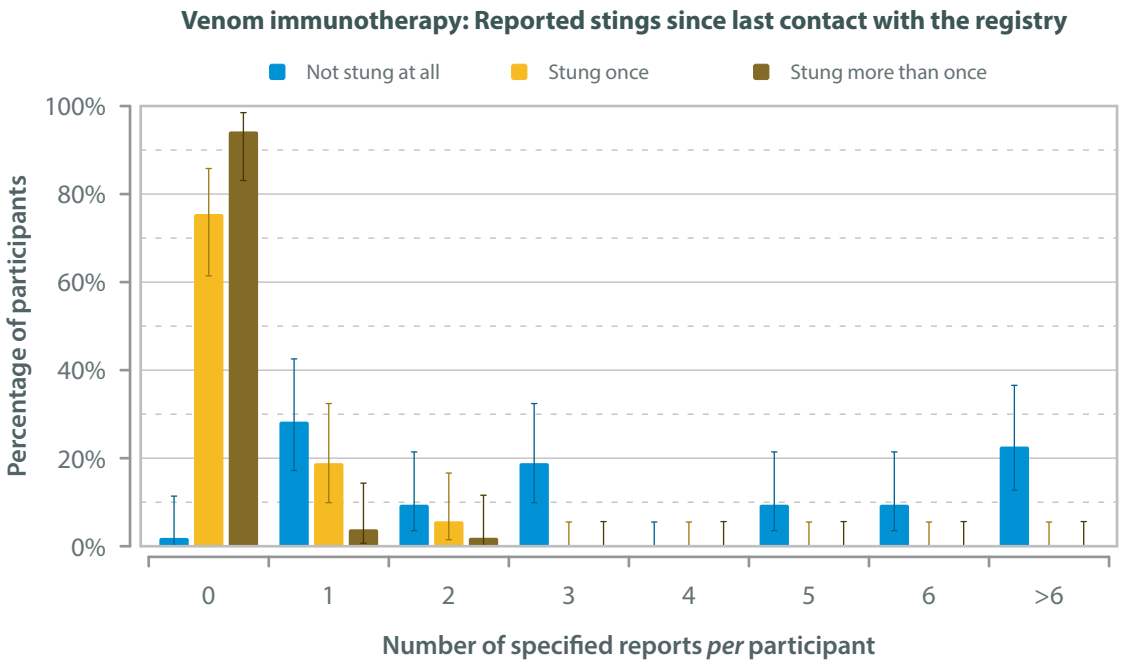
All were related to immunotherapy; both patients recovered.

i. Used where brands are switched during maintenance (Nasser et al. CEA 2019) [23].
ii. Pharmalgen, Venomil.

Effectiveness of venom immunotherapy

Reported stings

BRIT keeps track of response to field stings. Participants are asked to complete a quality-of-life questionnaire annually and to record if there have been any accidental stings and the reaction that those stings caused. This is a novel example of the real world effectiveness of venom immunotherapy. BRIT had 23 positive reports of field stings returned and 273 no-sting reports.



Reaction to reported sting

Of 23 reported stings in patients receiving venom immunotherapy, no participants required adrenaline. Most were mild and did not require treatment. This is a considerable improvement from generalised severe allergic reactions that prompted the use of venom immunotherapy in these individuals.

Venom immunotherapy: responses to reported stings

		Count	Percentage of responses
Reaction to any reported stings	No more than a normal sting	10	43.5%
	Reaction at the site – did not need any treatment	3	13.0%
	Reaction at the site needed treatment	9	39.1%
	Allergic reaction – did not need adrenaline injection	1	4.3%
	Allergic reaction – needed adrenaline injection	0	0.0%
	Responses	**23**	
	Participants	**15**	

Omalizumab

Overview

BRIT also has the capability to record and track response to Omalizumab for the treatment of Chronic Spontaneous Urticaria. There has been less take up of this part of the registry, but its capability shows how novel monoclonals may be incorporated in due course.

Prior treatment

NICE Guidelines recommend the use of Omalizumab as an optional add-on therapy for treating severe chronic spontaneous urticaria in adults and young people aged 12 years and over (TA339, 2015). NICE recommends that use of OMA is reserved for secondary care centres specialising in dermatology, immunology and allergy, who use objective measures of disease severity to track response. Courses should be stopped by the fourth dose if there is no response and discontinued at dose 6 if there is complete response; Omalizumab can be restarted if there is a relapse.

Before starting a patient on this treatment regime, standard treatment with H1-antihistamines and leukotriene receptor antagonists should have been tried, and a lack of response demonstrated to these medications.

Omalizumab for CSU: prior treatments

		Count	Percentage of participants
What treatments have been tried before starting Omalizumab	None	0	0.0%
	Standard dose H1 antihistamines	2	10.5%
	High dose H1 antihistamines	19	100.0%
	H2 antihistamines	7	36.8%
	Leukotriene antagonists	11	57.9%
	Prednisolone	13	68.4%
	Cyclosporin	2	10.5%
	Other	4	21.1%
	Unspecified	1	
	All participants	**20**	

Treatment

16 participants had 18 treatments recorded.

All treatments were 300 mg × 4 weeks; none were home treatment.

5 treatments had stopped (4 participants).

Of the stopped courses, 3 / 5 completed the recommended course; 1 / 5 stopped because of poor adherence; 0 / 5 new asthma; 0 / 5 side effects as a reason for stopping.

The reason for stopping the fifth treatment was not indicated.

Discussion and references

Discussion

The BSACI Registry for Immunotherapy is the first prospective registry of its kind for specific immunotherapy (SIT). Since its launch the registry has shown steady uptake by paediatric and adult allergy services. A picture of the clinical use of SIT is starting to emerge and will increasingly reflect national prescribing. The registry maintains communication with patients who have been discharged from specialist services, so for the first time we will be able to monitor the real-world effectiveness of treatment both during and after SIT. Most importantly we can also monitor the safety of allergen immunotherapy to guide practice.

There have been previous surveys of the clinical use of immunotherapy. Vance *et al.* undertook a retrospective evaluation of the use of paediatric SIT across 12 centres in the United Kingdom with data on 323 children [25]. A similar study has been conducted for adult centres in the United Kingdom [26]. They recorded data from 22 adult centres by retrospective questionnaire and captured information on 1,731 SCIT and 741 SLIT patients with results that are comparable to those emerging from BRIT. Prospective web-based surveys have also been used to evaluate the safety of SIT. The European Survey on Adverse Systemic Reactions in Allergen Immunotherapy (EASSI) recorded data from clinics in France, Germany and Spain [27]. They recorded data on 4,316 patients from 112 physicians with a systemic reaction rate of approximately 2% predominantly associated with SCIT. All of these surveys provide useful snap shots but do not record ongoing care. Chronic urticaria has been the focus of registry development with the global CURE registry collecting data for 39 sites and 2,946 individuals [28].

BRIT records any serious adverse events related to treatment, and all adverse events that lead to the cessation of treatment. These stopping events don't have to be severe; they may be mild but persistent, and lead to poor adherence and breakdown of treatment. The BRIT adverse event reporting structure will allow comparison of its data with other large data sets by mapping symptoms to the Medical Dictionary for Regulatory Activities (MedDRA). The registry coding was built on the EASSI MedRA coding for SIT adverse events [19]. BRIT uses the standard anaphylaxis severity gradings of the WAO but also uses a BC definition for anaphylaxis, as this enables a more accurate assessment of causality [18, 20]. We have mapped additional MedRA terms to make incorporation of both of these anaphylaxis definitions possible. In addition we have mapped further MedRA terms used for reporting omalizumab adverse events [29], and for local injection site reactions based upon the Brighton Collaboration case definition [22]. BRIT has developed a comprehensive panel of MedRA terms to enable accurate reporting of adverse events related to SIT and omalizumab therapy.

There are several further unique aspects to this registry. Firstly, BRIT is designed to enable healthcare users to access data on their own patients so that they can use registry data for local purposes, as a guide for individual clinical treatment, for service evaluations and quality reporting. Other registries do not provide data access for the centres that contribute data [28]. This provides little incentive to contribute timely and accurate clinical information over the long-term. BRIT is working with IQAS to provide centres the ability to download reports for their activity for RCP accreditation. We plan to work toward greater patient participant engagement in the second phase of development. Secondly, although the registry is built upon single consultant-based services, there is facility to work in teams across several different consultants and hospital sites, and to delegate data entry to nursing and junior medical staff. This reflects how consultants currently work within the NHS. Thirdly, BRIT has been designed to simplify data entry and to confine it to clinically relevant material [30]. Once familiar with the requirements entering data on a new participant takes less than five minutes.

Although there has been steady uptake, BRIT still has a long way to go. There has been better engagement from paediatric centres than in adult care. Paediatricians are used to working across clinical networks. Paediatric services tend to be smaller than adult centres and can see the advantages of collaboration for their own practice. BRIT was recently adopted by the RCP adult allergy quality standards IQAS and is recommended for centres who wish to meet their standards for centre accreditation. We expect to see increased engagement of adult services as the registry becomes better known. There are few participants in the devolved nations; the majority of participants live in England. This is not related to treatment of patients in the larger centres in London as the majority of participants live outside of that area. There may be a paucity of SIT provision outside of England. BRIT will help to map services and will be able to document how far the patient had to travel to receive their care, as well as residential IMD codes to investigate socio-economic disadvantage.

Immunotherapy is not a static landscape and BRIT will adapt and change to reflect current clinical practice. In the short time since its launch it has already managed the withdrawal of Pharmalgen [23]. The future of BRIT will also need to encompass the use of SIT for food allergy, initially by oral and epicutaneous routes for treating peanut allergy [31]. It is our aim that the registry will have become an important tool for mapping allergy services in the United Kingdom and will help us to meet the *unmet need* for care [32]. Allergen specific immunotherapy is at the heart of what allergists offer. The data from the registry will map provision of services and chart real world effectiveness and safety for our patients.

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The First Registry for Immunotherapy Report

We can do more for our patients when we work together. It has long been acknowledged that immunotherapy , despite being a highly efficacious treatment, is underused in the United Kingdom and we have a large, unserved group of patients with a significant burden of unnecessary disease. If we are going to convince commissioners of this need and bring about genuine change for our patients then there are a number of tasks we have to fulfil. Research, through large scale randomised controlled trials and systematic reviews, have already done the job of proving the efficacy of immunotherapy but it is only through real world evidence of acceptability, safety and effectiveness that we will have the tools that we need. There is, of course, some value in the data collected from single specialist centres but when we come together to form registries such as BRIT and develop a true community of practitioners from across the country in both specialist and non-specialist environment, then we have far greater power. The BRIT registry is an extraordinarily important opportunity to harness this power for the good of our patients and it is critical that we all see it as our responsibility to play a role in this. This report is a fantastic start at demonstrating just what we can achieve. I look forward to all of us being active contributors to what will no doubt be considered, in a few years' time when we look back, as a real watershed moment for our specialty.

Professor Adam Fox, President, BSACI

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