

BSACI Registry for Immunotherapy (BRIT): *Providing safe and effective immunotherapy for allergies and urticaria*

1 | INTRODUCTION

Immunomodulatory therapies alter the natural course of allergic and autoimmune disease and have cemented their place in clinical management. National audits involving paediatric and adult allergy services have identified heterogeneity in patient selection and vaccine use for allergen-specific immunotherapy (AIT) for allergic rhinitis in the United Kingdom (UK) National Health Service (NHS).^{1,2} This problem is compounded by the 'unmet need' for specialist allergy services and the huge burden of allergic disease. Despite pioneering strides and ground-breaking translational research, the delivery of AIT in the UK NHS has lagged behind other countries. In the last three decades, demographics of UK population have changed due to increased immigration. Despite state funding free at point of care, there is inequity in healthcare and patient-related outcomes in non-white populations. Furthermore, recent research has highlighted an enhanced risk of allergic and autoimmune disorders in the non-White British populations.³ In order to address these important concerns regarding equity and standardization of care, the British Society for Allergy and Clinical Immunology (BSACI) launched the BRIT (BSACI Registry for ImmunoTherapy) registry in 2018 to capture real-time prospective data on AIT and use of immunomodulatory treatments for allergic diseases and chronic spontaneous urticaria (CSU). In this editorial, we aim to describe the BRIT registry and highlight the publication of its first report.⁴ The report also shows how national registry data can provide high-quality evidence of 'real-world' clinical effectiveness of immunomodulatory therapies as highlighted by the European Academy of Allergy and Clinical Immunology (EAACI).⁵

2 | WHAT IS BRIT?

BSACI Registry for ImmunoTherapy is a secure online prospective registry for monitoring the effectiveness and safety of AIT for allergic rhinitis and hymenoptera venom allergy and biologic treatment for CSU in children and adults. The registry captures real-time data including demographics, patient selection, co-morbidities including asthma, safety and efficacy parameters. The first report published this month provides evidence regarding some heterogeneity in AIT

practice in the UK as reported in previous paediatric and adult national audits.^{1,2}

BSACI Registry for ImmunoTherapy was launched in October 2018, and by the time of its first report in May 2020, there were 101 registered consultant users and 76 delegated users (nurse specialists and junior doctors) from 65 centres. At that point, BRIT received greater engagement from paediatric allergy services; it is anticipated that adult services will start contributing since the national accreditation program (*Improving Quality in Allergy Services*, IQAS) mandates engagement with the registry. A majority of participants reside in England (both in and outside of Greater London) with very few participants from devolved nations. About 55% of referrals were from secondary and tertiary care, with a third from primary care and the rest were either self-referrals or remained unspecified. To date, 78.7% of participants received AIT for allergic rhinitis, 17.8% received venom immunotherapy (VIT), and 3.5% were on omalizumab for CSU. Of patients with allergic rhinitis, three quarters had seasonal symptoms; one-third had perennial symptoms and a small proportion (12%) received treatment for asthma. Although similar numbers of patients received subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) using grass pollen extracts, SLIT use predominated for tree and house dust mite allergens. 46% and 26% of SLIT and SCIT participants respectively had chronic well-controlled asthma. Only 3 of 87 (3.7%) of patients who had allergy to animal dander received AIT. There were 20 recorded adverse events in participants receiving AIT (overall rate 4.4%) with more in those concurrently receiving SCIT and SLIT. The combined number of adverse reactions for SCIT and SLIT amounted to 31 with a single report (3%) of anaphylaxis. A total of 103 patients received VIT (predominantly against wasp) with 23 reported field stings, but none required use of adrenaline. Twenty patients (3.5%) were on omalizumab for CSU with all patients having failed high-dose antihistamines and 13 (68.4%) required oral prednisolone therapy.

3 | HOW DOES BRIT COMPARE WITH OTHER REGISTRIES?

Prospective web-based surveys have been used to evaluate safety of AIT. The European Survey on Adverse Systemic Reactions in

Allergen Immunotherapy (EASSI) recorded data in France, Germany and Spain involving 4,316 patients from 112 physicians with 2% systemic reaction rate predominantly with SCIT.⁶ Over time, the European Anaphylaxis Registry, Mastocytosis Registry (European Competence Network on Mastocytosis, ECNM) and the primary immunodeficiency registries such as UK-PID or ESID (European Society for Immunodeficiencies) have played significant roles in identifying prognostic variables that have enabled personalized care. Chronic spontaneous urticaria has been the focus of registry development with the global CURE (Chronic Urticaria REgistry) registry collecting data from 39 sites and 2,946 individuals.⁷ Most surveys provide useful snap shots but do not record on going care in a prospective manner. In contrast, BRIT collects prospective data with participants contributing real world effectiveness and safety data both during and after treatment.

4 | ADVANTAGES OF BRIT

The BRIT Registry aims to generate regular national level data summarizing demographics, clinical effectiveness, safety and access to AIT and biologics for allergies and CSU. It is envisaged that this data will shape national policies with respect to workforce, resource allocation and help to achieve the much-needed equity and standardization of allergy services in the UK. For instance, at present, there are no UK data regarding safety and effectiveness of VIT and BSACI guidelines are based on data published from Europe and North America. BRIT aims to address this important gap, including VIT in patients with clonal mast cell disorders.

BSACI Registry for ImmunoTherapy has been funded by pharma through unrestricted grants to our professional society. Sponsors do not have direct access to the data or serve on the steering group. Despite this indirect role there are considerable advantages to sponsors beyond that of a highly visible marketing opportunity. These include the ability to monitor the post licensing real world use of their products and their safety and effectiveness. We are working with pharmacovigilance teams to establish anonymous adverse event reports. Companies will also be able to easily identify the professional immunotherapy community in the UK through its engagement with the registry.

The value of the dataset is already apparent. An important observation has been made in the first annual BRIT Report. As per current BSACI guidelines, chronic well-controlled asthma is a relative contraindication for AIT in allergic rhinitis. Interestingly, the registry has highlighted that nearly a third of patients receiving AIT are on BTS/SIGN step 3 or above therapy for asthma.

The use of biologic treatment for severe CSU has gathered momentum in the UK NHS in recent years and is based on National Institute of Health and Clinical Excellence (NICE) guidelines. Recent UK experience suggests a requirement for multiple treatment courses in a majority of patients with severe CSU⁸ and use of treat-to-target concept⁹ may be better applied in biologic-resistant cases.

The BRIT registry provides an opportunity to generate such datasets prospectively to enable strategic planning of resource allocation for specialist allergy centres.

5 | CHALLENGES

The success of the BRIT registry, however, depends on the active long-term engagement of allergy services and patient participants. The commitment to the registry offers dividends for services in their ability to measure their own performance against national level data and assist towards recognition by IQAS.

Not least of these challenges are the data protection and governance of a national registry containing identifiable and commercially sensitive information. The registry is governed by a steering committee consisting of BSACI members alongside IQAS and two patient organizations (Allergy UK and Anaphylaxis Campaign). Robust governance framework aligns with General Data Protection Regulation (GDPR) and demands the written informed consent of participants contributing personal data. Consultant users have immediate access to their patient participant's data and can use them to feedback response to treatment to their patients and for departmental service evaluation. No one person or group has access to all of the data. Requests for analysis and data export for specific purposes are reviewed by the steering committee and final data generated contain non-identifiable data.

A logic model highlights some of the challenges the allergy community faces and how the registry aims to address them with defined outcome measures of success (Figure 1). This model is akin to quality and clinical governance employed by Pathology services which mandate participation in national external quality assurance schemes (UK-NEQAS) for diagnostic tests wherever available (Pathology Quality Assurance Dashboard: second Edition, NHS England & NHS Improvement, November 2019).

6 | FUTURE

The BRIT registry presents a great opportunity to improve quality of care for immunomodulatory therapies for allergies and CSU in the UK. For the first time, a prospective national registry will demonstrate clinical effectiveness and safety of 'real-world' use of these expensive treatments in the UK NHS and will facilitate standardized and equitable clinical care. It will also allow centres to benchmark themselves against national trends and encourage adherence to current guidelines. The registry is a flexible platform that engages patients directly in their care. It has already adapted to changes in venom and AIT in the UK and we envisage this will further evolve as new treatments become available. The BRIT registry is a great example of a successful collaborative multi-professional initiative between a national clinical and scientific society, patients and patient support organizations.

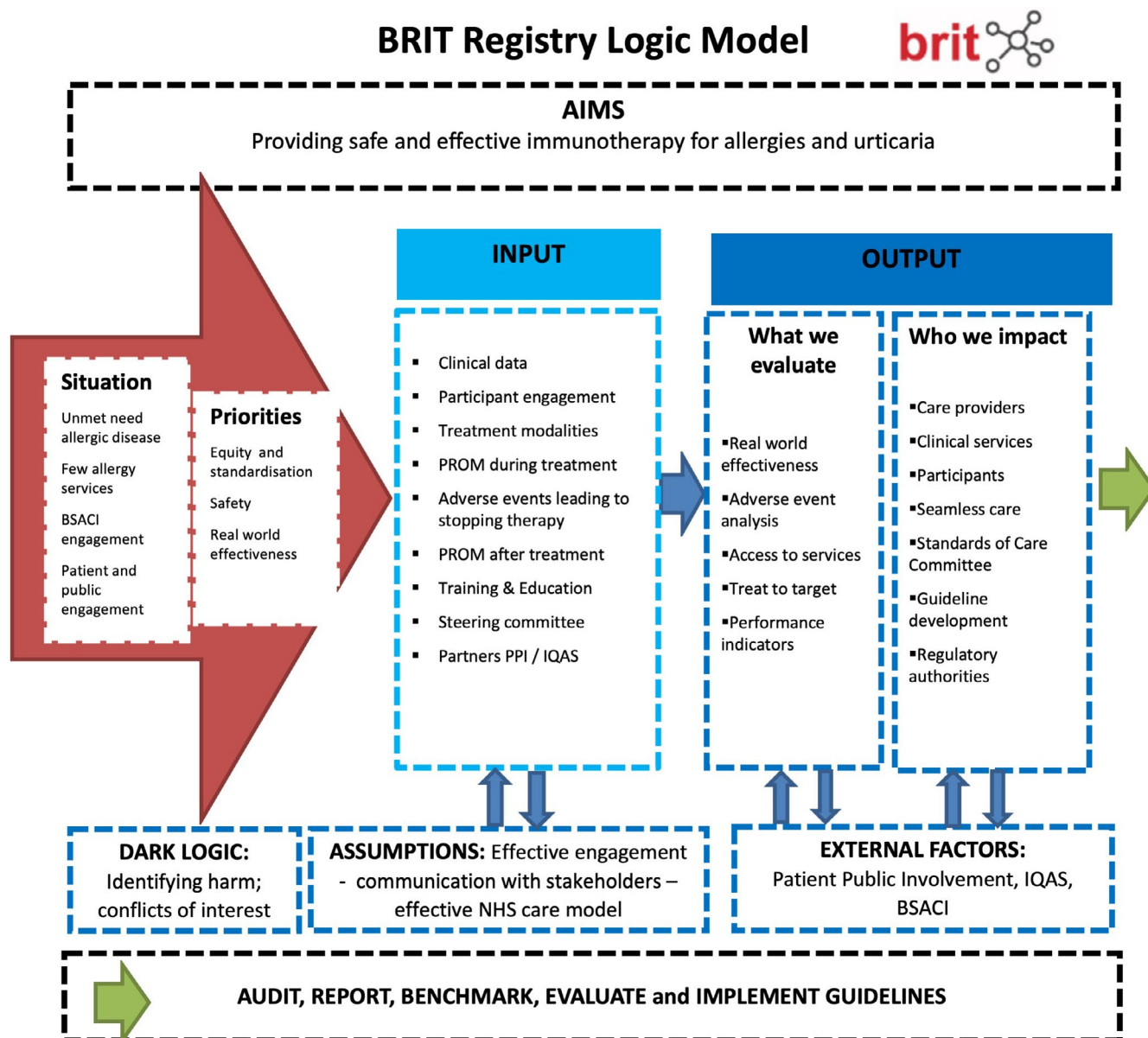


FIGURE 1 The BRIT Registry Logic Model shows the potential of a professional and patient interface to address gaps in safety and effectiveness of immunotherapy in allergies and urticaria. Governing bodies are ideal organisations to host such registries, but 'assumed' shared priorities will help address the challenges allowing real-world effectiveness data to be available on demand. With careful evaluation of key markers of success ('What we evaluate') and achievement ('Who we impact'), centres will be able to make informed decisions as to how to allocate resources for clinical services

CONFLICT OF INTEREST

Dr Khan is a member of the Steering Committee of the BSACI British Registry for Immunotherapy and Technical Assessor for Immunology & Allergy for United Kingdom Accreditation Services (UKAS). Prof MT Krishna received funds from ALK-Abellø to attend an international conference. He is clinical lead for the national allergy accreditation programme (IQAS) and chair of BSACI Equality Diversity and Inclusivity working group. He has received grants from NIHR, MRC CiC, FSA and UK R&I, unrelated to this work. His department received funds from ALK-Abellø, Thermo Fisher, MEDA and other pharmaceutical companies for PracticAllergy course.

Dr Michaelis reports that she is the Paediatric Secretary of the BSACI British Registry for Immunotherapy; Principal Investigator and educational grants from Danone Nutricia, and Regeneron and previous educational grants from Allergy Therapeutics and ALK-Abellø. Dr Dawson reports that he has received educational grants from Allergy Therapeutics, Danone Nutricia and ALK-Abellø ADD and is a member of Registry steering committee. Dr Anna Thurby-Pelham, Dr Leyla Pur Özyiğith and Deborah Marriage are members of the Steering Committee of the BSACI British Registry for Immunotherapy. Carla Jones is the Patient and Public Voice representative on the NHS England and NHS Improvement Immunology

and Allergy Clinical Reference Group. She is a patient representative on the IQAS accreditation programme. Allergy UK receives grants and sponsorship from a range of companies which support the patient organization projects and activities. Companies which Allergy UK has worked with in the last 12 months in relation to immunotherapy are Aimmune, ALK, DBV and ThermoFisher. Dr. Erlewyn-Lajeunesse reports that he is chair of the BSACI British Registry for Immunotherapy ADD and has undertaken scientific advisory work for Aimmune and DBV Technologies.

AUTHOR CONTRIBUTION

The article was written by Dr Khan, Prof Krishna, Dr Michaelis and Dr Erlewyn-Lajeunesse. Prof Krishna and Dr Michaelis contributed equally in this respect. As the current registry steering group, all authors contributed to the ideas that framed the work and reviewed draft and final versions.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

FUNDING INFORMATION

The BSACI has received educational grants from Allergy Therapeutics, ALK-Abellø, and Stallergenes Greer to support the registry.

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