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**Food Allergy among Irish Children:
An Exploration of the Risk and Impact of Accidental Allergic
Reactions**

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On research carried out with the School of Medicine, Trinity College Dublin AND Department of
Paediatric Allergy, Crumlin's Health Ireland at Crumlin, and Tallaght.

Supervised by Dr Aideen Byrne

Declaration

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work.

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The work contained within this thesis work is my own. I confirm I did receive statistics support for parts of chapter 5 (Section 5.4 results).

I confirm that full and informed consent was obtained from human subjects.

A handwritten signature in black ink, appearing to read 'M. Crealey'.

Signed

Dr Miranda Crealey

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Summary

Introduction

Food allergy (FA) now impacts almost 1 in 20 Irish children. These children are at risk of allergic reactions and anaphylaxis. Food is an integral part of all social activities, and thus children with FA are at risk of exclusion or over supervision at these events. The burden of FA among Irish children has not previously been defined. Parents and food allergic children attending our service are educated in how to minimise risk and avoid accidental reactions; we promote safe, age appropriate, social interaction and eating practices. However, there is a paucity of evidence based educational interventions to support newly diagnosed parents.

The aims of this project on Irish food allergic children are (i) to establish the social practices and eating out habits of these children (ii) to report their incidence of accidental allergic reactions and (iii) design an educational tool using this information and assess its impact.

Methods

This thesis is comprised of 2 studies:

Chapters 1-4

A prospective observational study “ReAACT” (Recording Accidental Allergic Reactions in Children) was established, enrolling food allergic Irish children aged 2 to 16 years with confirmed FA. Data was collected between November 2018 and May 2020 from two tertiary allergy sites- Children’s Health Ireland at Crumlin and Tallaght with a catchment area of Leinster and surrounding counties. At enrolment, information on social activities and eating out habits was collected by questionnaire both retrospectively and also prospectively at 3 monthly contacts. Participants were contacted at 3 monthly intervals for 1yr to prospectively report accidental allergic reactions (AARs) to food. (Chapter 5)

We built on the results of ReACCT by using data collected to design an educational booklet. Subsequently, a prospective RCT enrolling parents of newly diagnosed nut allergy was established with this booklet as the intervention. Participants completed 4 questionnaires both before and after the intervention.

Results

(Chapter 1-4)

531 children were enrolled, and allergic reaction data was reported on 498. These children are attending age-appropriate social activities; (e.g. 5-12 yr olds: 302 (97%) go to birthday parties and

272 (85%) to friend's houses). Overall, 523 (98 %) were visiting food establishments. Among those who did not participate in social activities, significantly more had a previous history of anaphylaxis (RR 1.44, 95% CI 0.97 to 2.14; p=0.06).

We report a high annual incidence of allergic reactions as 0.44 (95% CI 0.38-0.50); 155(31.1%) reported at least one reaction in the year. Overall 31 (14%) of the reactions were graded as anaphylaxis; only 12 of 31 (39%) received intramuscular adrenaline. In 77 (35%) reactions, the allergen was unidentified. Schools were unprepared to manage FA with only half having a FA policy and less than two thirds of children had an emergency plan there, however those that did had a significantly lower risk of a reaction (RR 0.2, 95% CI 0.09-0.47, P=0.0002).

Chapter 5

Within the subsequent RCT with a separate patient cohort, there were 20 participants in the intervention group and 15 in the control group. We found a significant improvement in quality-of-life scores, anxiety score as well as an improvement in self-efficacy scores in parents who had received the educational tool booklet intervention.

Conclusion

Irish children with FA are "living with allergy" ; they attend age-appropriate social activities and visit food establishments. The annual incidence of reactions is 0.44 (95% CI, 0.39 to 0.48) is high, however most were mild, non-anaphylaxis reactions (n= 189, 86%). Only 21/31 (39%) of anaphylaxis cases were administered intramuscular adrenaline. Nearly half of reactions were caused by unintentional administration by parents. This highlights the difficulty in relying on avoidance to manage FA as well as highlighting the ongoing need for education on avoidance strategies. A low cost, low intensity educational intervention in the form of a booklet was effective at improving quality of life and anxiety in parents of newly diagnosed children with nut allergy, a tool which can be rolled out with immediately in our clinic.

Lay abstract

This thesis is comprised of 2 studies:

- (1) A study where food allergic children were observed for 1 year for allergic reactions
- (2) An assessment of the benefit of an educational booklet for parents with a nut allergic child

The number of young children with food allergy, is increasing worldwide. These children are at risk of allergic reactions. A diagnosis of food allergy can cause much anxiety in parents. They worry about their child being exposed to foods they are allergic to when outside the home. This anxiety can lead to these young children avoiding taking part from taking part in normal childhood activities such as attending parties, friends' houses and eating out.

We enrolled a sample of 531 children attending two allergy clinics (CHI at Crumlin and Tallaght) between 2 and 16 years of age into this study. We collected information on social activities, eating out habits and attendance at school and childcare; we monitored for allergic reactions for 1 year. We found that these children with food allergy are "living with food allergy". They are going to parties, visiting friend's houses, and taking part in activities. However, accidental allergic reactions are frequent with about 1 in 3 children having a reaction in a year. The majority of reactions are mild and not life threatening. We found that just over one third of participants are using their emergency medication for a severe reaction. Half of reactions occur at home and with the parent present. However, children are also having reactions in schools and childcare settings; There is a suboptimal approach to food allergy management in these settings. We also found that just over one third of participants are using their emergency medication for a severe reaction.

We then built upon these results by using the findings to develop an educational booklet to help to lessen the fear and anxiety experienced by parents of young children with newly diagnosed nut allergy. We imagine that knowledge of how other families with children who have food allergy participate in activities involving food outside of the home might help newly diagnosed families. We performed a different study with parents of children with a new diagnosis of nut allergy. Half of them were given the educational booklet and the other half did not. We found that those who received the booklet had an improvement in anxiety levels, a better ability to enjoy and participate in life and improved belief in their ability to manage food allergy in their child.

The findings provide a unique insight into the life of children with food allergy in Ireland. They will enable improvement of current services and planning of future services.

Research questions and aims

Research questions:

1. What are the behaviours of Irish food allergic children in respect to social participation and eating out in food establishments?
2. What are the practices within Irish school and preschool childcare facilities with regards to food allergy ?
3. What is the annualised rate of accidental allergic reactions in Irish children and adolescents who attend an allergy clinic?
4. Is an educational booklet effective at decreasing the burden in parents of newly diagnosed nut allergic children?

Research aims:

1. To report the social practices and eating out habits of Irish food allergic children and adolescents.
2. To establish the annual incidence rate of accidental allergic reactions to food in Irish children already identified as food allergic.
3. To identify contributing factors for accidental reactions
4. To use the data collected to design an educational tool for use by parents of newly diagnosed nut allergic young children.

Research objects:

1. To identify and recruit food allergic children for this study
2. To collect relevant background data
3. To record at regular intervals all accidental reactions and the events surrounding them
4. To interview in detail all patients who experience accidental anaphylactic reactions.
5. To design an educational booklet using the data collected
6. To assess its effectiveness in parents of young children newly diagnosed with nut allergy.

Value of my research

Up until now, there has been little known on the burden of FA among Irish food allergic children. This work gives us a unique insight into many aspects of FA in Irish children and adolescents. It explores their social functioning, eating out habits, as well as the FA practices within Irish schools and preschool childcare settings, on which no data has previously been available. As well as that, there is no Irish data on allergic reactions in children. There is also no published literature review on accidental allergic reactions (AARs) in children and there is a limited number of large studies from other countries with robust FA and AAR definitions, done prospectively. The information that is collected as part of this study, will allow us, as clinicians to provide parents with relevant, valid, local information that will help them to risk assess in different environments, to contextualise the risk that FA places on their child and by doing so come closer to achieving the delicate balance between over protection and endangerment.

The results of this project, have the ability to make a real difference for food allergic children in Ireland. They will allow us, going forward, to inform key stakeholders in the care of children in the public, such as Tusla (Child and Family Agency), Department of Health and Department of Education in Ireland and advise with regards to AARs in Irish day cares, schools and after school environments.

We have used the data collected to design an educational booklet for parents of newly diagnosed nut allergic children. This novel technique has not been used previously in the allergy literature. Such a low-cost intervention has the capacity to make a real difference in clinical practice without the need for high intensity resources. It has the potential to improve health related quality of life, anxiety levels and self efficacy in parents of children with FA- in particular newly diagnosed young children with nut allergy and is a huge value of this research.

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List of abbreviations

| | |
|----------|--|
| AAI | Adrenaline autoinjector |
| AAP | Allergy Action Plan |
| AAR | Accidental allergic reaction |
| AH | Antihistamine |
| BASELINE | Babies After SCOPE: Evaluating the Longitudinal Impact using Neurological and Nutritional Impact |
| CHI | Children's Health Ireland |
| CI | Confidence Interval |
| CSS | Childcare service |
| EAACI | European association of allergy and clinical immunology |
| ED | Emergency department |
| FA | Food allergy |
| FAIM | Food allergy independent measure |
| FAP | Food Allergy POLicy |
| FAQLQ-PF | Food Allergy Quality of Life Questionnaire parental proxy form |
| FAQL-PB | Food allergy quality of life parental burden form |
| FASEQ | Food allergy self-efficacy questionnaire |
| FE | Food establishments |
| G1 | Group 1 |
| G2 | Group 2 |
| G3 | Group 3 |
| HRQoL | Health related quality of life |
| IFAN | Irish Food Allergy Network |
| Inh | Inhaler |
| NIAID | National Institute of Allergy and Infectious Disease |
| OFC | Oral food challenge |
| OIT | Oral immunotherapy |
| PN | Peanut |
| QoL | Quality of Life |
| Qn | Questionnaire |
| RCT | Randomised Control trial |
| SE | Self Efficacy |
| splgE | Specific IgE |
| STAI | State and trait anxiety inventory |
| TN | Treenut |

Research outputs to date

Oral presentations

“Visiting food establishments: behaviour patterns in food allergic Irish children”.

Paediatric Allergy and Asthma Meeting (PAAM) Florence, Italy. (October 2019)

“Involvement of food allergic children in social activities attending an allergy service”.

Paediatric Allergy and Asthma Meeting (PAAM) Florence, Italy. (October 2019)

Poster presentations

Are adolescents with food allergy participating in social activities?

Food allergy and Anaphylaxis meeting (FAAM), Online (October 2020)

Accidental allergic reactions in Irish children attending an allergy clinic

European Allergy and Clinical Immunology (EAACI) annual conference, Online (July 2021)

Accidental allergic reactions on vacation: Are they lost in translation?

European Allergy and Clinical Immunology (EAACI) annual conference, Online (July 2021)

Irish schools: an uncommon location for accidental allergic reactions.

Paediatric Allergy and Asthma Meeting (PAAM), Online (November 2021)

Prizes

1. Awarded best poster prize for my presentation at International Conference Food Allergy and Anaphylaxis Meeting (FAAM) October 2020.
2. Awarded best poster prize for my presentation at International Conference Paediatric Allergy and Asthma Meeting (PAAM) November 2021.

3. Runner up for William Stokes research Price, National Doctors in Training Day, Royal College of Physicians, May 2022.

Published abstracts

Prospective observational study of accidental allergic reactions amongst Irish children and adolescents. Crealey M, Byrne A. Allergy 2021 Vol. 76 Issue S110 Pages 571-572
DOI: <https://doi.org/10.1111/all.15096>

Accidental allergic reactions on vacation: Are they lost in translation? Crealey M, Byrne A. Allergy 2021 Vol. 76 Issue S110 Pages 542-543. DOI: <https://doi.org/10.1111/all.15096>

Manuscript in preparation

The effectiveness of a novel educational tool for parents of newly diagnosed nut allergic young children. M Crealey, A Dunn Galvin, A Byrne

Chapter 1: Introduction and baseline data

Section 1.1 : STRUCTURE OF THE THESIS

This thesis comprises of 2 studies examining risk and impact of accidental allergic reactions in Irish food allergic children. The first is a large prospective observational study involving 531 children and adolescents (chapters one-four). The second is a RCT involving 97 parents of young children (chapter five)

Chapter 1 introduces the reader to the study, setting the scene for the remaining chapters. It described the primary methods of the study. It provides some baseline data results on the demographic and clinical characteristics of the participants.

Chapter 2 examines participation in social activities and attendance at food establishments. The introduction to this topic, is followed by a literature review. There is a brief additional methods section. Relevant results from ReAACT are then reported with a subsequent discussion.

Chapter 3 addresses accidental allergic reactions. The chapter begins with an expanded introduction, beyond that provided in chapter 1. A comprehensive literature review follows. The methods section describes the methodology relevant to this section. Detailed results from ReAACT are reported and discussed.

Chapter 4 outlines attendance at school and preschool childcare services and accidental allergic reactions that occur there. There is a brief introduction to the topic with a literature review. The methods described in chapter 1 are relevant for this chapter. Results from ReAACT are then reported and discussed.

Chapter 5 describes on the educational tool RCT. The introduction introduces this tool and the background to it. There is a literature review on the topic. A methods section follows giving a full account of its methodology. The results are reported and consequently discussed

Chapter 6 Summary of the thesis

Section 1.2: INTRODUCTION

Prevalence of food allergy

FA is increasingly common worldwide. Based on data from oral food challenges (OFCs), a 2013 survey of allergy organizations found that the prevalence of FA ranged from 1% to 10% among infants and preschool-age children and 1% to 2.5% in children over the age of 5 years of age (1) (1). More recent research suggests the prevalence may now be higher in some populations of older children (2). From the Babies After SCOPE: Evaluating the Longitudinal Impact using Neurological and Nutritional Impact (BASELINE) cohort study, we know that 4% of Irish infants now have FA (3). Children with FA are at risk of developing life-threatening reactions, especially those with unresolved milk and or egg allergy, and those with nut and seed allergy. Anaphylaxis rates are also reportedly increasing worldwide (4), however the low rate of fatalities from anaphylaxis remains remarkably stable (0.5-1%) (5).

Risk of accidental allergic reactions

The risk of a severe allergic reaction, including the rare risk of anaphylaxis, is an enormous psychological weight for parents and children to carry (6). It is the reason that the quality of life for allergic families may be poor and why they experience isolation (7). FA may also limit children's participation in day-to-day activities and put them at risk of allergy-related bullying (8). Novel therapies including immunotherapy are on the horizon for some allergens, however, currently, avoidance remains the mainstay of management in Ireland. Indeed, avoidance may remain a viable option for long-term management of FA for many, given the significantly higher rates of allergic reaction to therapies such as peanut oral immunotherapy (OIT) versus avoidance demonstrated in nearly all clinical trials (9).

Paediatric allergy services in Ireland

Paediatric allergy is an emerging speciality in Ireland. At the time of this study's commencement (November 2018), the Children's Health Ireland (CHI) Allergy service was provided from 2 of the 3 Dublin paediatric hospital sites; Crumlin and Tallaght. These two connected services provided allergy paediatric care to all patients referred from Dublin city and the greater Dublin area as well as the province of Leinster and surrounding counties. Leinster is the most densely populous of the provinces in Ireland with a population of 2,630,720 (10) . CHI at Crumlin also provided tertiary allergy services for complex allergy cases from Munster and also northern counties within the

Republic of Ireland (Figure 1.1). The rest of the food allergic children in Ireland were primarily seen in Cork University Hospital with small numbers also seen in Galway University Hospital and Portlaoise.

Figure 1.2.1: Map of Ireland



Figure 1.2.1 legend: This shows a map of Ireland with 28 counties in the Republic of Ireland. Dublin is highlighted in navy. The counties incorporating the province Leinster are Dublin, Meath, Westmeath, Kildare, Wicklow, Carlow, Kilkenny, Laois, Longford, Louth, Offaly, and Wexford.

Source: Department of Housing, Local government, and Heritage.

Food allergy education

All patients attending the CHI allergy service receive education and a comprehensive management plan from the allergy team (allergists and allergy trainees, allergy clinical nurse specialists and dietician). This is standardised across both sites. At the time of commencement of this study, this programme included the following: : allergen avoidance strategies, how to read food labels, how to recognise an allergic reaction and assess severity, how to treat an allergic reaction, how to use an allergen autoinjector (if applicable). Advice is individualised and is dependent on the age of the child and the allergens involved. All families are given a written allergy action plan (appendix) and a trainer adrenaline autoinjector (AAI) (if applicable). Parents also receive a letter to give to the school or preschool childcare service, stating their child has been prescribed AAIs. The Irish Food Allergy network (IFAN) website is a source of further

information. All of the advice provided is based on international evidence and recommendations. Previous work in other countries, highlights the effectiveness of such an education programme. Ewan et al report a 60% reduction in severe reactions in food allergic children in receipt of such a management plan and adrenaline prescription based on risk (11). Kappoor et al found that after one visit to the paediatric allergy clinic, there was a significant improvement in parental knowledge of allergen avoidance (26.9%, $P < 0.001$), managing allergic reactions (185.4%, $P < 0.0001$) and AAI usage (83.3%, $P < 0.001$). Additionally, there was a significant reduction in allergic reactions ($P < 0.001$) (12).

Requirement for local data

A key part of the education of our allergic families is in becoming effective risk assessors. This requires information, not only specific to the individual patient but also data on the overall risk of inadvertent exposure. The BASELINE cohort study from Cork has provided us with invaluable prevalence data of FA in Irish 2-year-olds (3). However, currently the only data available on annual incidence of allergic reactions is from other countries and is conflicting with rates of between 3 and 50% (13-18). This will be discussed in detail in chapter 4. The different figures are more likely to be due to the differences in both the environment within which they were collected and the methodology of the study, rather than being incorrect. The fact that reaction risk figures cannot be applied outside of the environment within which they were calculated is demonstrated clearly by a study from Massachusetts which showed a significant difference in the incidence of anaphylaxis between schools with peanut free lunch tables and those that did not separate children. However, they failed to demonstrate a difference between schools that served or did not serve peanut (19). Thus to advise parents correctly, it is imperative that accurate local figures are collected.

To do this, we need to have correct information on the environment that these children are living in and collect information on their social behaviours, eating out habits and Irish school FA practices. This data will give us an insight into FA within Irish society as well as providing context within which AARs are occurring. It is also essential that in the design of this type of study that there is attention placed on ensuring that all children enrolled are truly still food allergic at the time of enrolment, as most children outgrow their milk and egg allergy and 10 to 20% of nut allergy will also resolve. Enrolment of non-allergic children would risk under estimation of accidental reactions.

Thus, to properly care for the increasing numbers of food allergic Irish children, ensuring their safety and at the same time their social inclusion, a prospective study of accidental allergic reactions (AARs) to food, in a well-defined population of food allergic children, is necessary. With limited access to allergy services in Ireland, the parents of FA children have relied on a range of information resources. Many online resources accessed by Irish people are not evidenced based. FA stories reported by the Irish media, particularly the 3 fatal anaphylaxis cases we have had in Ireland in the last decade have had a deep impact on the psyche of Irish people. It is important that we provide a story which counteracts the negative bias that the national media has towards FA.

Rationale for this study

The information that is collected as part of this prospective study, will allow us, as clinicians to provide parents with relevant, valid, local information that will help them to risk stratify in different environments, to contextualise the risk that FA places on their child and by doing so come closer to achieving the delicate balance between over protection and endangerment. We feel confident, that this in turn will contribute to improving the quality of life of our patient cohort.

In addition, this study cohort represents the vast majority of patients seen in the Dublin allergy clinics; it includes 25% of children between 2-16 years of age already reviewed in the CHI allergy service in 2018. Their avoidance practice and response to accidental reactions will be representative of the training that we provide in our clinic and thus provide us with a platform for continued improvement in quality of or emergency preparedness training.

These results of this project, have the ability to make a real difference for FA children in Ireland. They will allow us, going forward, to inform key stake holders in the care of children in the public, such as Tusla (child and family agency), Department of Health and Department of Education advise with regards to AARs in Irish day cares, schools and after school environments. Data reported within chapters 2 to 4 has also been used to design an educational tool for parents of newly diagnosed nut allergic young children. This tool will be discussed in chapter 5.

Section 1.3: METHODS

Introduction

A prospective observational study- “Recording Accidental Allergic Reactions in Children and Teenagers” (ReAACT) was established in November 2018. What follows is a description of the methodology for ReAACT. Much of this section is applicable to chapter 2-4 and should be referred to while reading these chapters.

Study sites

This was a multisite study, incorporating two tertiary referral allergy centres- Children’s Health Ireland (CHI) at Crumlin and Tallaght as discussed in the introduction. All patients attending the allergy clinics at these sites have their food allergies diagnosis evaluated and confirmed by international best practice through a combination of standardised history taking, testing and oral food challenges (OFCs). Protocols for performing skin prick testing (SPT) and open food challenges have been standardised across the two centres. Similarly, training on food allergen avoidance and emergency readiness is standardised across the two clinics allowing for recruitment from both sites.

Participant identification

To be enrolled in the study, children attending the CHI allergy service needed to fulfil the following inclusion criteria.

The inclusion criteria were:

1. Age

Children had to be >2 years but less than 17years of age. Children with FA tend to also have atopic dermatitis (eczema) as genetic eczema (e.g. filagrin mutation). Atopic dermatitis is the first step in the allergic march and a high risk factor for the development of FA. In infancy, eczema is at its most active, triggering regular pruritus, often acutely with variable cutaneous erythema thus making it more difficult for parents to correctly differentiate between acute allergic reactions and eczematous flares. Similarly, perioral reactions to histamine releasing and topically irritating foods such as tomato are very common in infants and commonly mistaken for IgE mediated food allergic reactions. It was decided, in light of this, to exclude infants < 2 years

of age, in order to minimise recording of non-immediate or non-IgE mediated food allergic reactions. In addition, almost all of our patients under the age of 2 are engaged in active programs for reintroduction of dairy and or egg via ladder models. Furthermore, most of those under 15months are still in engaged in allergen first exposure programs. The nature of these programs, are that non accidental allergic reactions are relatively common (20) . Furthermore, the distribution of atopic dermatitis in young atopic infants is primarily facial especially in boys (21). Inflamed perioral atopic dermatitis combined with messy early feeding behaviours leads to high numbers of perioral erythematous reactions, due to contact reactions (22)and/ or response to direct histamine release from tomato based foods etc. All of the factors outlined above highlight the regularity of reactions in this cohort. In order to accurately differentiate accidental food allergic reactions from non specific contact, reactions due to trials of food on egg and milk ladders and to new foods would require a prospective daily diary model with frequent contact (weekly) with study team.

Participants were <17 as this is the upper age limit for referral to CHI Crumlin and Tallaght.

2. Diagnosis of IgE mediated food allergy.

Children recruited to this study had a confirmed diagnosis of immediate type IgE mediated FA to common food allergens: cow's milk, hen's egg, peanut, tree nuts, fish, kiwi, seeds. More unusual/rare allergies to foods rarely encountered in childhood such as singular allergy to shellfish, caviar for example, were not included. However, if children allergic to a common food allergen were also allergic to an unusual food allergen, these were included. Children with both singular and multiple food allergies were included.

Participants were defined as having a diagnosis of IgE mediated FA if either of the following 4 criteria were met at study entry:

(i) a clear history of a recent reaction (previous 6 months) clinically consistent with immediate IgE mediated allergy and a positive skin test >3mm

or

(ii) a history of a reaction in the past (not necessarily the recent past) and a skin test in the past 6 months to that allergen, of >7mm

or

(iii) a positive OFC performed at CHI Tallaght or CHI Crumlin in the past 6 months.

or

(iv) a history of a reaction in the recent past (previous 6 months) and evidence of sensitisation to a non-specific lipid storage protein (LPS)

This strict study inclusion criteria ensured that participants were still food allergic at study entry. Clinical history and evidence of sensitisation alongside OFCs are the mainstay for the diagnosis of FA.

The exclusion criteria were:

1. < 2years or >16 years
2. An isolated diagnosis of non-IgE mediated FA (e.g. Eosinophilic oesophagitis or food protein induced enterocolitis) or pollen food syndrome. Pollen food syndrome can occur in patients with seasonal allergic rhinitis; they experience allergic symptoms on eating certain plant foods as a consequence of clinical cross-reactivity with homologous epitopes found in them (23).
3. Cow's milk (CM) and/or hen's egg allergy on the IFAN cow's milk or hen's egg ladder without evidence of a recent reaction. Many children attending the allergy services were on the milk and IFAN cow's milk and hen's egg ladders. Children with an isolated CM and or egg allergy on a ladder without a recent reaction were not included. Access to OFCs is limited in our service and are not routinely done in children on ladders. Children with singular unusual food allergies were also not included.
4. Participation in another research study

5. A diagnosis of a condition that can be difficult to differentiate from acute allergic reactions such as Physical or Idiopathic Urticaria, Cutaneous or Systemic Mastocytosis, very severe or difficult to control atopic dermatitis. The study did include numerous multisystem allergic children with eczema, including those with severe eczema on biological therapy. We considered that it might be difficult to accurately assess immediate type reactions in the uncontrolled eczema group. There was only one child who was excluded from participation due to uncontrolled atopic eczema during recruitment.

6. Children with a significant or complex medical history such as cystic fibrosis or developmental delay. We considered these children's behaviours and activities would not be representative of the general allergy population. Children with chronic conditions have decreased social functioning (24). They might also have excessive levels of supervision not in keeping with other children of their age. We did include children with autistic spectrum disorder.

Participant recruitment

Participants and their parents were recruited from the allergy clinics and day ward at CHI Tallaght and the allergy clinic and day ward at CHI Crumlin. Patients who had attended the clinic in the past 6 months had their case notes reviewed. If they met the study criteria, they were contacted. Both new and return patients were recruited. Participants were recruited over 7 months (November 2018 to May 2019). As reaction risk, type of food ingested, and environment, are different at different ages, recruitment was to 3 age subgroups: group 1 (G1), 2-4 years of age, group 2 (G2), 5-12 years of age and group 3 (G3), 13-16 years of age.

Process of recruitment and consent:

Parents and participants were recruited by two methods:

1. During clinic and day ward attendances (in person).

Parents were provided with details of the study, by the study team both verbally and in written format, in the form of the patient information leaflet (PIL) (see appendix). This included: background and rationale for doing the study, the benefits of taking part the study, data to be collected. It was made clear that study participation was voluntary, that refusal to participate did not affect their child's clinical care in any way and that participants could withdraw from the study at any stage. Parents were approached in the waiting room at clinic attendance or in the day ward. Families had sufficient time to read the information and have questions answered while waiting for skin testing to be measured/interpreted and while awaiting education. If agreeable, the consent form was signed by the parent and then collected by the study team.

2. Outside of clinic appointments (over the phone).

Parents were contacted and invited to participate if they have attended the allergy service in the last 6 months and met the inclusion and exclusion criteria. Verbal information was given over the phone and the PIL and consent form along with a stamp addressed envelope (SAE) were sent by post. These parents were contacted again 2-3 days after the initial phone call to answer any questions and clarify participation. Verbal consent was provided, and written consent forms were returned in the SAE via post to CHI Crumlin.

Baseline data collection

A 42-item baseline questionnaire was completed with the parent and patient (Appendix) in the form of a structured patient interview and combined with information from the participants medical record. It gathered the following information:

Demographic information: age, sex, ethnicity as per Irish census identifiers (White Irish or White non-Irish, Black or Black Irish, Asian or Asian Irish) , mother and father's occupation, single parent home, number of siblings, living environment (urban or rural). Lived in emergency accommodation during the study period (Emergency accommodation is that which is provided to those that have become homeless). The term ethnic minority described all participants from Black/Black Irish and Asian/Asian Irish ethnicities.

Clinical information: confirmed food allergies, history of anaphylaxis; associated atopic conditions, eczema, asthma, and allergic rhinitis (AR). A previous history of anaphylaxis was self-reported. This was recalled by parents and was backed up by evidence from clinical notes in most cases. Receipt of the standardised education and training (as described in section 1.1) was checked for all participants. If there were any concerns over a participant's education, they were directed towards the clinical team for further education. No additional training or advice was provided as part of this study. Thus, patients who did not take part in ReAACT were not disadvantaged.

Details of their childcare plan/schooling anticipated for the following year: (School: primary, secondary, creche/minder, after school,). Details from their school regarding eating policy "nut free", eating at separate tables, storage of adrenaline autoinjectors was collected.

Details of participation in social activities and eating out: attendance at parties, friend's houses, extracurricular activities (ECA), visits at food establishments, routine practices at cultural holidays (e.g. Easter and Christmas).

Details of holidays planned: mode of transport, destination.

Once recruited into the study participants were followed for one year. All participants were contacted at 3 monthly intervals (4 contacts in total) by phone to collect information on accidental allergic reactions (AARs) (The methodology relevant to this is described in detail in chapter 4). At these contacts, parents were asked if there was any change in the frequency of going to eateries, their child's participation in ECAs, attendance at parties or friends' houses, or their stage in school. If there was a change, this was noted. If there was a change in the age group, this was changed and was reported as their category within the study, i.e. participants could not be in more than one age/school category at a time but could be within different groups at different study intervals.

Data collection period: November 2018 and May 2020.

A proportion of participants were still being followed at the onset of the first wave of the COVID-19 pandemic and the associated lockdown that was imposed. In Ireland all schools and preschool CCS were closed from 13th March 2020. All social gatherings were banned from March 24th with food establishments only operating take away from that date (25, 26). Participants who had ended their 1-year follow-up on or before 12th March 2020 were deemed to have been

followed during “normal circumstances”. Reaction data collected between 12th March and May 30th 2020 was deemed to be during “unusual circumstances” as the country was in lockdown.

Data management

Data was stored on an encrypted and password protected Excel datasheet. Data was transferred to SPSS version 27 (2018; SPSS Inc., Chicago, IL, USA) for analysis. All participants were assigned a study ID number. Data was pseudo-anonymised. The consent form contained the participants name and their ID number and thus represented the code to unlock the anonymisation of the data. It was stored in a secure location within the Allergy research office in CHI at Crumlin. As participants had to be contacted throughout the study, it was not possible to have the data completely anonymised. Only the participant’s study ID number was linked with other data sources (data sheets, allergic reactions data etc) thus representing linked anonymity.

Ethics

Ethics approval was received from both the Research Ethics Committees (REC) in CHI at Crumlin (REC Reference: GEN/672/18) and CHI at Tallaght (SJH/TUH REC) (REC Reference: 2018-09 Chairman’s Action (6)).

Sample size calculation

The total population of patients aged 2-16 years attending the allergy clinics in both sites amounted to 2095 at the time of study commencement in 2018. A sample size calculation on this total population with confidence level of 95 and interval of 5 % was 325. We increased the level to 99 with an interval of 5%, the sample size was 505 to calculate the AAR in the group as a whole.

The total population of children with FA attending our service was subdivided into 3 age groups: G1 (2-4 years): 582; G2 (5-12 years): 1222; G3 (13-16 years): 291. A sample size calculation on each of these 3 groups was done. The sample size necessary for a confidence level of 95 and interval of 5 for each age group was calculated: G1: n=232; G2: n=294; G3: n=166.

Data analysis

Data was inputted into Microsoft Excel and then into SPSS (version 27: 2020; SPSS Inc., Chicago, IL, USA for analysis). Data was cleaned using SPSS “detect duplicate cases” tabs. Then, descriptive statistics were compiled for all variables to ensure the data made sense.

Demographic and clinical characteristics were compared using two-sample t-tests or Wilcoxon rank-sum tests for continuous variables and Fisher’s exact or chi-squared tests for categorical variables, as appropriate. Continuous variables were visually assessed for normality using histograms. For normally distributed data, mean and standard deviation was reported. For data with a skewed distribution, median, lower and upper quartiles were reported. All tests were two-sided, and significance was set at 0.05. To ensure a high level of accuracy, confidence intervals were set at 95% and the study was powered at 80%. A $P < 0.05$ was considered statistically significant. Proportional differences between categorical variables were calculated by using relative risks (RR) as this was a prospective study.

Section 1.4: RESULTS

Subject enrolment and data collection

Process of data collection over the one-year study period

Five hundred and thirty-five patients between 2 and 16 years were enrolled into REACT over a 7-month period (November 2018 to May 2019). After enrolment, there were 4 dropouts. These 4 were consented to take part in the study but were unable to be contacted by phone to complete the initial questionnaire; therefore they were considered “dropouts”. Consequently, baseline demographic details and clinical characteristics were collected on 531 children. (Table 1.3.1). Thirty-three participants were lost to follow up; We were unable to contact them after collection of initial baseline data (Figure 1.4.1). Therefore allergic reaction data was collected on 498 children. Overall, there were 324 participants who were followed for a full 12 months during normal circumstances.

Figure 1.4.1: Flow of participants

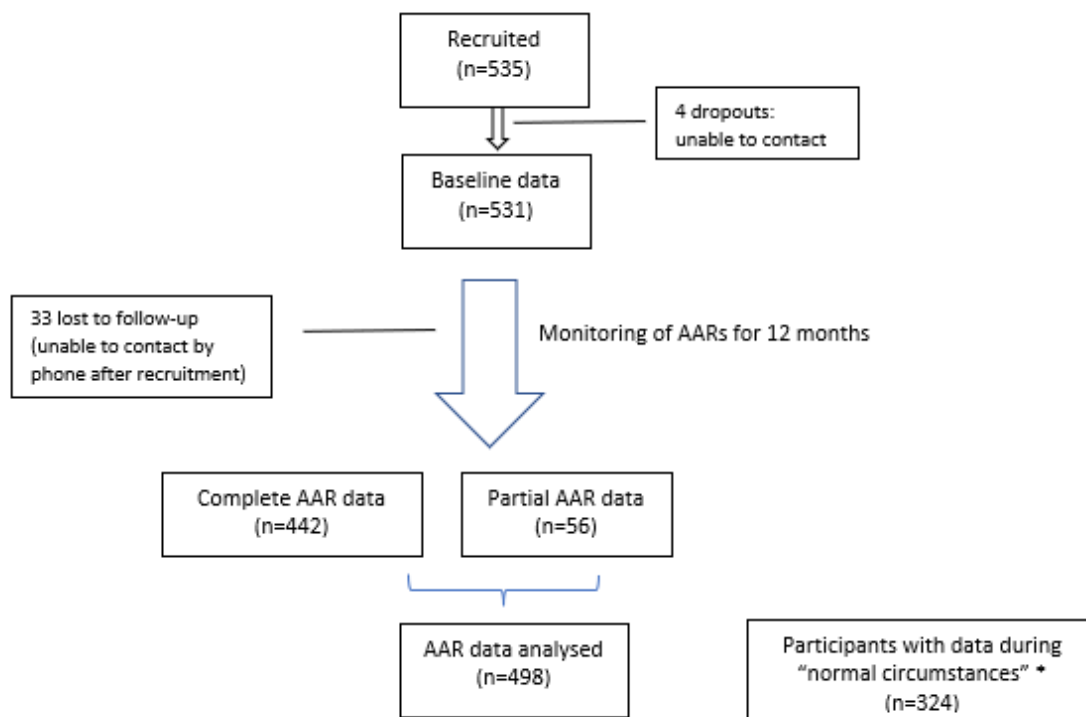


Figure 1.4.1 legend: This shows the flow of participants through the study.

*Normal circumstances: participants who had a full 12 months follow up prior to the covid-19 pandemic and lockdowns

Abbreviation: AAR: accidental allergic reactions.

Of the 531 participants, just under half (45%) were recruited over the phone with the remaining 55% recruited in person. In total 4744 calls were made by one researcher to both recruit patients and then to collect data on AARs over the study period. There was a total of 5 attempted contacts with each participant (1 at recruitment to collect baseline data, 4 follow up calls at each quarter to check for AARs). Three attempts to contact participants by phone were made at each quarter. There were a number of recruits that could not be contacted, and this resulted in missing data for that quarter. Over the 1-year period of observation for AARs, 442 (88.8%) participants were able to be contacted at 4/4 of their 3-month follow-ups, 34 (6.8%) at 3/4 follow-ups, 13 (2.6%) at 2/4 follow-ups and 9 (1.8%) participants were able to be contacted at 1/4 follow-up phone call. Nineteen (3.8%) participants were uncontactable at the end of their 4th quarter (12 months timepoint). All of these participants were contacted subsequently between 6-9 months later to check for AARs during their last quarter in the study.

Participants were contacted a mean of 2.1 times at each quarter before data could be collected. Of the 531 enrolled, the participant's father was the primary contact in 75 (14.1%). In only 10 (2%) cases, did both the mother and father provide data. In 488 (98%) of cases, the same parent was spoken to on all 5 occasions.

Subject characteristics

Of the 531 participants recruited, the median age was 7 years (LQ 4, UQ 10). Participants were divided into 3 groups based on their age. Group 2 (G2) (5-12 yrs) accounted for more than half of the total (n=310, 58%); Group 1 (G1), the preschool aged group (2-4 yrs) accounted for just over a quarter (n=141, 27%) with the adolescents in group 3 (13-16 yrs) making up the remainder (n=80, 15%). The number in each group reflected the age breakdown within the clinic population.

Over two thirds (66.1%) were male. The majority of participants (n=447, 85%) were of Irish Celtic origin (Table 1.4.1). The majority (n=432, 82%) lived in urban areas; only 2 participants had lived in emergency accommodation during the study period. Over 90% of families had between 1 and 3 children.

97% had at least one other co-existing atopic condition; eczema (n=265, 49%), asthma (n=221, 42%), allergic rhinitis (n=330, 62%). Over two thirds (67%) had 2 or more FAs. Peanut (64%) and treenut (48%) were the most predominant allergens with a third of participants allergic to hen's egg (33%). A number of participants with common FAs also were allergic to less common allergens e.g. pulses (n=42, 7.9%), fruit (n=46, 8.6%), shellfish (n=17), wheat (n=7), chicken (n=5), coconut (n=6), soya (n=3). During recruitment, no child were found or excluded for having a singular unusual FA. 10% of individual who had IgE symptoms to the more common allergens also had PFS. Of note, 2 participants were sensitised to non-specific lipid transfer proteins which had been the cause of allergic reactions in the past. A quarter (25%) of participants reported they had a history of anaphylaxis. Overall, 9 (1.7%) participants had a diagnosis of autistic spectrum disorder (ASD).

Table 1.4.1: Baseline characteristics of participants

| | Participants with baseline data (n=531) N (%) | Participants monitored for reactions* (n=498) N (%) |
|--|--|--|
| Gender n (%) | | |
| Male | 355 (67) | 344 (69) |
| Female | 176 (33) | 154 (31) |
| Median age at recruitment (yr) (LQ, UQ) | 7 (4, 10) | 7 (4, 10) |
| G1 n(%) | 141 (27) | 131 (26) |
| G2 n(%) | 310 (58) | 291 (58) |
| G3 n(%) | 80 (15) | 76 (15) |
| Ethnicity n (%) | | |
| White: Irish | 447 (85) | 415 (83.3) |
| White: Non-Irish | 38(7) | 39 (7.8) |
| Black or Black Irish | 10 (2) | 9 (1.8) |
| Asian or Asian Irish | 36 (6) | 35 (7) |
| Number of food allergies n (%) | | |
| 1 food allergy | 174 (33) | 167 (33.5) |
| ≥ 2 food allergies | 357 (67) | 331 (66.5) |
| Food allergens n (%) | | |
| Cow's milk | 79 (15) | 77 (15) |
| Hen's egg | 187 (35) | 182 (36) |
| Peanut | 339 (64) | 315(60) |
| Treenut | 258 (48) | 248 (49) |
| Fish | 50 (9.5) | 40 (9) |
| Previous history of anaphylaxis n(%) | 134 (25) | 135 (27) |
| Other atopic conditions n(%) | | |
| Eczema | 265 (49) | 255 (51) |
| Asthma | 221 (42) | 224 (45) |
| Allergic rhinitis | 330 (62) | 300(60) |
| Number of allergic co-morbidities | | |
| 1 | 146 (27) | 128 (26) |
| ≥ 2 | 385 (73) | 370 (74) |
| Environment n(%) | | |
| Urban (city, town) | 432 (82) | 402 (81) |
| Rural (farm, isolated) | 99 (18) | 96 (19) |
| Family size (including child) n(%) | | |
| 2 | 35 (6.6) | 26 (5.6) |
| 3-5 | 481 (90.6) | 460 (92) |
| ≥6 | 15 (2.8) | 12 (2.4) |
| Single parent household n(%) | 35 (6.6) | 32 (6.4) |
| If yes: single mother | 31 (88.6) | 30 (93.7) |
| Emergency accommodation at any time during the study n(%) | 2 (0.3) | 2 |
| * This was the total number of participants who had full or partial data for reaction monitoring and will be described in chapter 3. | | |

Section 1.5 DISCUSSION

This large prospective study of 531 participants is the largest Irish observational study of food allergic children and adolescents to date. It provides local, real-life data on a whole range of elements of FA Irish children and adolescents. It not only establishes norms for Ireland but also facilitates comparison with studies from other countries on FA children.

We believe this cohort to be representative of FA children in Ireland. As outlined in the introduction, due to the evolving nature of Allergy services in Ireland, the CHI allergy service is currently referred and accepts all cases of FA in Leinster. At the time of recruitment there were 2050 children registered as patients of the service, from which the study cohort (n=531) was recruited.

Demographic details

Over two thirds of participants were male which is consistent with American and Canadian observational studies of food allergic children (27, 28) but differs from other studies of Australian or British populations of food allergic children (2, 29). The ethnicity of this study population reflects that of the general Irish population with Irish Caucasian (85%) making up 85% of the ReAACT population and 82.5% of the Irish population (30). The other 15 % were from minority groups. There is a growing evidence base on the disparities that exist in FA management among ethnic minorities which is likely due to a number of social determinants such as education, access to food and social contexts (31). This study was not designed specifically to examine the risk of accidental food reaction in children from minority groups but data from those gathered is analysed separately in subsequent chapters.

Some of the demographics of this study population differed from that of the general Irish population. 82% described themselves as living in an urban area. This is higher than the national average of 63% (10). However, the higher number of urban dwellers is due to the catchment area of the allergy service being primarily urban as outlined in the introduction.

Over 90% of families had between 1 and 3 children which is reflective of the national norm. The average number of children per family in Ireland has remained at 1.38 over the last decade (32). A minority of families (6.6%) described themselves as one-parent families which is just under 3 times less than the number within the general population (18%) (32). Single parenthood is strongly associated with lower socioeconomic (SE) status in many populations (33, 34). In contrast FA is associated with higher SE status (35) so one might conclude that it is not unexpected that

there is a lower number of single parent families among these food allergic families. However, it must be remembered that there is little FA knowledge in more deprived areas where single parent families are more common (36) and this may account for the lower numbers in this study.

The current housing crisis in Ireland has caused the number of homeless people in Ireland to rise (>8000 since 2020, 532 families) (37) due to the lack of affordable rental accommodation and social housing. It was therefore important to identify how many of the study population were in emergency accommodation at any point during the year in the study. Living in cramped, shared living quarters poses another challenge for FA families, one which 2 participants (0.37%) had to cope with in this study. In 2018, there was an estimated 0.3% of 1 million <15 yr olds living in emergency accommodation (32). Therefore, 2/531 is overrepresented in comparison to the general population.

We included children with autism spectrum disorder (ASD), of which there were 9 (1.7%). This is similar to the most recent estimate of prevalence in the Irish population of 1.5% (38). In contrast, an American population-based study recently found an increase in self-reported FA in children with ASD (39).

Definition of food allergy

FA is strongly associated with other atopic conditions and 97% of the ReAACT population had a co-existing atopic condition. Other populations recruited from allergy clinics in other countries have similarly high rates of atopy e.g. eczema (51-70%), asthma (43.5-57.7%) .

The definition of FA used in a study impacts on the results and the comparability of the study. The gold standard of FA diagnosis is the Oral Food Challenge (OFC) (40). However, it is not always feasible to achieve this standard, due to resource limitations and participant reluctance. Kelleher et al recently developed a new algorithm for the diagnosis of IgE-mediated FA in clinical studies of young children relying on clinical history and/or SPT in the absence of availability of OFC and showed it reliably excluded FA (41). This study's onset preceded this development.

All of our patients had both a history of a reaction and evidence of sensitisation by skin prick test. In particular, those with cow's milk and hen's egg allergy had to have a history of a recent reaction. A substantial proportion (25%) reported at least one episode of anaphylaxis prior to study commencement. This was retrospective self-reported data, so it may overestimate the actual

incidence of past anaphylaxis. A thorough analysis of symptom profile for all reported cases was possible for most participants.

Clinical characteristics

The profile of food allergies is comparative to other international studies, Kapoor et al did find quite a similar distribution of FA in their UK allergy clinic population with a median age of 6 years: (PN 61%, TN 54.8%, cow's milk 19.4%, hen's egg 33.1, fish 12.4%)(12). In our study, in which the median age was 7yr, the distribution was remarkably similar as displayed in Table 1.31. Almost half of our study population had a tree nut allergy and 64% had a peanut allergy. This corresponds with what we understand about tree nut allergy prevalence from other populations. The Australian HealthNuts group has shown that the prevalence of tree nut allergy is the same as peanut allergy at 6 years (42). The prevalence of cow's milk and hen's egg allergy is unsurprisingly lower than in the Baseline study, whose cohort were all infants. We only included children with a recent cow's milk or hen's egg reaction as allergic to either protein. Complete Resolution of these allergens is common by age 4-5 years (43, 44) and SPT correlates poorly with clinical reactivity (45).

Emerging food allergies in Ireland such as pulses (7.9%) and fruit 8.6%) were also represented in the study. It is important to note that fruit can be a cause of anaphylaxis, with kiwi, banana and mango being the most common culprits (46).

Over two thirds of our study population had 2 or more FA. This is comparable with other study populations worldwide, recruited from allergy clinics, with similar median ages, e.g. British populations (47-71%) (11, 12), American populations (75-79%) (47), Canadian populations (45.9%) (18).

FA is strongly associated with other atopic conditions and 97% of the ReAACT population had a co-existing atopic condition. Other populations recruited from allergy clinics in other countries have similarly high rates of atopy e.g. eczema (51-70%), asthma (43.5-57.7%) (15, 17, 28, 48, 49) .

Data collection

The original recruitment consent and collection of baseline data occurred with the participant's mother in 85% of cases. This was unintended, however in each case either the child attended with their mother, or her contact details were listed as first next of Kin. In much of Irish society, the

mother retains the role of primary caregiver irrespective of her employment status and therefore data collection from her likely enhanced data correctness. Similarly, a UK based study found that 62.1% of paediatric patients attend with their mother (50).

Conclusion

The purpose of this chapter was to provide some background to allergy in Ireland and also to set the scene for the upcoming chapters. By providing the demographics of the participants, we allow the reader to understand how this population compares with, firstly the general Irish population and also to the populations of allergic children seen in allergy clinics worldwide. The recruited population are representative of the wider Irish childhood population, and food allergic study populations in the western world. The following chapters build on this information and provide a unique insight into food allergic children and adolescents in Ireland.

Chapter 2: Social activities and eating out practices of Irish food allergic children

Section 2.1: INTRODUCTION

In order to study accidental reactions in food allergic children it is first essential to gain an insight into the food related practices of the population.

Food is an integral part of most social activities, for children just as with adults. Childhood social engagements such as parties, play dates and sporting activities have food associated with them. All-important family celebrations tend to be marked by the preparation and sharing of food. Similarly, cultural events are marked by traditional meals or specific foods and treats. Furthermore, visiting food establishments is an essential part of modern family life. Birthdays and weddings and other important life events are often celebrated in such places. Eating outside of the home is now a regular family practice. Understanding the degree to which FA children and their families partake in all of these activities is critical to any evaluation of accidental reactions. It cannot be presumed that the practice of this cohort is similar to that of other children and families. Parents and carers of FA children perceive a risk from food related activities and their coping strategies can include avoidance and restriction.

Furthermore, it cannot be that that the social practices recorded in one country or environment are applicable elsewhere or remain similar over time. Social activities are influenced by culture, disposable income, working practices, changing trends etc.

Irish societal activities

In just over a generation, the fabric of family life in Ireland has changed to reflect more that of our neighbours. Ireland evolved from one of the poorest countries in Western Europe to one of the most successful with a thriving economy, increased living standards with the second highest gross domestic product (GDP) per capita in Europe in 2006. The worldwide crash of 2007 brought the country into recession. Nevertheless, the economy recovered and in 2020, Ireland had the 3rd highest GDP in the world (51). Irish families now have increased disposable income (net growth of 5.2% in 2019, 6th highest in the world) (52); the median household disposable income in 2019 was €43,552 (53).

This has resulted in a change in social habits. In particular, the Irish are eating out more. Irish households' spend 14.4% of their overall expenditure on catering services, which includes restaurants, takeaways, cafes, and canteens (data from 2018 spending) (54) which is more than double the EU average of 7 per cent.

In conjunction with this, a change in social structures has led to a decline in the average number of children per family from 1.82 in 1996 to 1.35 in 2016 (32). This provides families increased opportunity to involve children in social activities and eating out. Statistics on Irish children involvement in sports comes from peer and non-peer review.

The children's sport participation and physical activity study 2018 reported that 80% of primary and 58% of secondary school pupils reported participating in community sport (outside of school) at least once a week (55). Indeed, primary school aged children (5-12 yrs) in Ireland have one of the highest levels of physical activity among 42 WHO countries and regions, with almost 70% reporting 60 minutes of exercise 4/week (56). The longitudinal Growing up in Ireland cohort study found that three-quarters of nine-year-olds were involved in some form of organised sports club, the rate being higher among boys (84%) than girls (67%)(57) but this decreases to 28% at 13 years(58). However, these rates sharply decline in adolescence, with 45% of girls and 31% of boys reporting never taking part in community sport. A similar decline is seen in other populations (59).

Socialisation with peers by visiting their houses is another important activity for children and adolescents. Data from the Irish "Growing up in Ireland study" showed that 82% of 10 yr olds have 3 or more friends (56). There is little data on attendance at birthday parties. However, in 2016, a non-peer reviewed, Irish birthday party survey reported that inviting every child in the school class was common for children under 8yrs but that an average figure of approximately 11 were invited if the child is aged between 8 and 12yrs (60). It also found that most primary children are invited to an average 8 to 12 parties a year.

Food allergy and social activities

Children with FA are at risk of exclusion or over supervision during social activities due to anxiety around allergen exposure. In food establishments (FE) specifically, the risk of cross contamination of food products and the necessity to entrust to others the care or partial care of the child can propagate anxiety in parents (61). Exposure to new situations and social activities is integral to developing adaptive coping skills, social self-confidence, and healthy social relationships. Social isolation can result if food allergic children are prohibited from going to birthday parties, sleep overs and school trips (62). It is also interesting to note that following a negative food challenge, the social life of the child and family has been shown to significantly improve (63), which again highlights the potential negative impact that FA can have on social functioning.

Food allergy and eating in food establishments.

FA should not prohibit those with FA visiting and eating within FE. With appropriate planning and communication, as well as clear systems in place within FE, all food allergic consumers should be able to eat out in most types of restaurants. All food businesses have a legal obligation to provide safe food for their customers. FE in the EU are mandated under law to communicate with consumers about food allergens. EU legislation (EU FIC) introduced in December 2014 aimed to improve food allergen information provision for customers by requiring retailers of non-prepacked foods to provide written information related to the content of one or more of 14 specified food allergens within their foods. The Food Safety Authority in Ireland (FSAI) is the regulatory body that protects consumers and ensures compliance around food safety among eateries in Ireland. It provides guidance to eateries on how eateries can display allergen information.

Improvements in allergen information provision and raised awareness of FA in eating out venues in the UK, have been reported following this legislation (64). Unfortunately, this is not always the case. There was a high-profile media case in the UK in 2019, where a young man was asked by a restaurant to either bring his own food to the FE and pay a “corkage fee” to eat it there or to sign a disclaimer that his food was a risk of cross-contamination (65). As well as that, not providing or providing inaccurate written allergen information for customers was cited as one of the reasons Closure Orders were served on 7 Irish food businesses over 1 year (2017-8) (66). One of the goals of our allergy clinic is to empower the attending FA children and adolescents to participate in all aspects of life in a comparable way to their non allergic peers.

The **aims** of this chapter are:

1. To report on the practices of food allergic Irish children attending our service in relation to their involvement in social and family activities as well as visiting food establishments.
2. To consider the results in the context of available data on cultural norms within our society.
3. To identify areas for future education strategies.

SECTION 2.2: LITERATURE REVIEW

2.2.1 Introduction

This literature review examines what is currently known about the impact of FA on the social activities of children and their families. It specifically looks at the evidence concerning eating out, socialising and participation in activities.

2.2.2 Methods

Two searches were undertaken for this literature review.

(i) Participation in social activities

The following databases were searched for studies published in English: *PubMed*, Medline, Embase, Cochrane, PsycInfo, Cinahl and Web of Science. The following search terms were used: food allergy, food hypersensitivity, child, paediatric, pediatric, social, activit*,

(ii) Visiting food establishments

The following databases were searched for studies published in English: : *PubMed*, Medline, Embase, Cochrane, PsycInfo, Cinahl and Web of Science. The following search term were used: food allergy, food hypersensitivity, child, family, eat*, food consum*, restaurant, takeaway, food establishment,

2.2.3 Results

Part A: Participation in social activities

There is very little quantitative research looking at food allergic children's participation in social activities. Most research is qualitative which gives in-depth data but may not be representative. There is, however, a multitude of research on disease specific quality of life (QoL). Social limitations are one element that impacts QoL.

Participation of food allergic children in social activities

There is a paucity of data on the actual day to day activities of food allergic children. There are social limitations due to anxiety around allergen exposure and subsequent reactions. Springston et al found a wide range in levels of QoL among food allergic families, caregivers consistently reported being troubled by social limitations (67). An American study, which looked at how FA changes families' behaviours and activities, found that birthday parties, traveling, dining out and

entertainment activities present challenges for parents (68). More than half of parents have missed important school functions and 82% have changed family traditions to accommodate FA. The study by Bollinger et al provide data on the impact of FA on daily activities (69). This American paper uses their own unvalidated questionnaire, the food allergy impact scale (which included a child social activity subscale). It included 87 participants (mean age children 5.1yrs) recruited from a single university-based allergy clinic therefore reflecting a mostly homogenous population; it is not stated if they received training on allergen avoidance and FA management. They found that FA disrupts a variety of activities; 11% don't go to friends' houses, 11% don't do sports and 7% don't do other extracurricular activities. The biggest impact was on autonomous events with 26% not staying over in a friend's house, 26% not going to camp and 10% not going to birthday parties. However, a limitation of this study is that it does not provide the reader with any idea of the rates of these social activities within non-allergic children in the American setting. In addition, the mean age of the children of participants was 5.1 yrs (range 8 months-17yrs) so therefore sleep overs and camps are not age-appropriate activities for many of their participants. They also do not report, of those who attended social events, did they eat there. It was also performed almost 2 decades ago; times have changed since then.

Another American study used their specifically designed Social Activity Limitation Impact (SALI) questionnaire and recruited 293 participants from social media (70). This study found that the following activities were most limited: going to camp, going to friends' houses, , playing sports (practices, games), attending field trips and other extracurricular activities (e.g., scouts, clubs) (70). They also report that parents who are more worried and burdened by their child's FA were more likely to limit their child's activities even in situations of increased ability to monitor their child and that limitation of social activities may pose a burden on the family's QOL with increased parental burden reported. Activity limitation, particularly in settings where parents may perceive limited ability to monitor their child's safety, was associated with children's FA severity, including fewer recent reactions and hospitalizations. Indeed, mothers who have experienced anaphylaxis in their FA child are more likely to restrict a child's activities (71). A UK based study of 20 children found that those with peanut allergy felt more restricted in physical activities when compared to children with type 1 diabetes (7).

Two recent multicentre studies, in which participants were recruited from advocacy groups and recruitment companies APPEAL-1 and APPEAL-2 examined the involvement of children and teenagers with peanut allergy in social activities. APPEAL-1 was the quantitative study and included participants from Ireland. The total study population in APPEAL-1 was 1846 respondents, comprising 419 adults with peanut allergy (self-report), 546 caregivers who

answered for the child with PA (caregiver proxy-report) and 881 caregivers of a child with peanut allergy, who answered regarding the impact of peanut allergy on themselves. Parties and social gatherings posed difficulties with 67% reporting feeling restricted (72).

In APPEAL-2, the follow-on qualitative study, almost all children and teenagers reported a negative impact of peanut allergy on their social activities (73). For children and teens, using “avoidance” as a strategy of disease management included not only restaurants, but avoidance of certain places (e.g. cinemas) as well as missing activities with friends. Children and teenagers felt left out or envious due to being unable to attend social events and share food with others. These studies were done to highlight the difficulties that those with peanut allergy face. However, it is important to highlight that these difficulties were not universal, and a sizeable number of participants reported no or little restrictions in certain activities e.g. with regards socialising with friends, nearly 50% felt they were not restricted/mildly restricted because of their FA.

There is some evidence that food allergic children are “living an ordinary life with FA”. Alanne et al interviewed parents of food allergic 2-year-olds and found parents were getting on with life and planning around activities, however the authors do highlight that this may reflect a highly motivated and resourceful population that volunteered to take part in the study (74). This population contrasts with the previously mentioned studies which recruit self-selected populations who are more likely to be burdened by poorer QoL and less motivated. This raises the issues of parental personality and its influence on FA management. A paper examined personality traits (using the Big Five Inventory- John 1991) and ability to cope with everyday FA problems among adults (75). Counterintuitively, neuroticism did not predict more frequent allergy issues. Instead, higher openness to experience predicted a range of issues including anxiety at social situations and feeling excluded.

Calsbeek et al highlight that it may not be the medical condition itself that reduces participations but the mental health disorders associated with it (76). They looked at the burden of disease in various conditions including FA, in relation to participation in social activities in adolescents and young people and found that the medical diagnosis itself didn't have a significant impact on participation, but levels of depression associated with the condition did. In situations where a food allergic child or adolescent does participate in the social activity, the parent's behaviour or presence may be inappropriate for the child's developmental age. Some parents will accompany young children in social situations beyond the age at which non-allergic children might experience this (77).

There may also be difficulties in ability to socialise among food allergic children. Adolescents with FA are more likely to have insecure attachment and use avoidant strategies resulting in social

impairment (78). Parents of younger children report a more negative impact on social activities due to FA (71) with parents often having difficulties in trusting other caregivers. As well as the anxiety around situations involving food and the fear of a reaction inhibiting involvement in social activities, male teens with FA have been shown to have higher levels of anxiety related to all social situations (social anxiety), not just food related (79). As well as that, children with FA are more likely to be bullied (80). However, children with FA who participate in social activities such as camps report decreased anxiety and improved QOL (81).

Part B: Visiting food establishments

Another social challenge for children and adolescents with FA is eating in food establishments e.g. restaurants, cafes, takeaways, and fast-food establishments. The risk of cross contamination of food products; the necessity to entrust to others the care or partial care of the child; and the adequacy of labelling are some of the challenges encountered (61). There are a number of papers relevant to this area with one particular research team in UK (Lucas et al) providing most of the data.

The two main strategies parents and food allergic individuals have available to them are (i) avoidance of food establishments and (ii) communication (82). It is important to mention that a strategy that might keep a child safe in one place may not in another place. Different practices as well as varying legal requirements to display allergens, in different jurisdictions have an impact and will be discussed in more detail below.

Food allergic children visiting food establishments

There is little data available on the numbers of food allergic children and adolescents who actually visit eateries. One American study of 294 adults/caregivers recruited at an allergy conference, found rates of “never eat” for fast food to be 20%, informal dining 25%, and 19% for formal dining establishments (83). Another study from the USA, reported that 16% of families do not eat in restaurants because of their child’s FA (69). A recent American study of 206 parents via social media and an online survey company reported that 22% of food allergic children avoided eating takeaway food (84). Across a number of studies, there is a common theme: returning to the familiar eateries where their child had eaten on previous occasions (7, 61). Seeking familiarity is a key strategy used by nut allergic adults to reduce uncertainty and anxiety while eating out (82). Peterson et al reported that more than half of parents have left a restaurant while dining because of their child’s FA (70). Additionally, 89% always avoid certain types of restaurants e.g. Asian cuisine. To my knowledge, there is no data on how many of the food allergic individuals who visit eateries actually consume food while there.

Food allergy communication within food establishments

(i) Informing staff of FA

Appropriate communication between the FE and the food allergic child/parent is key to mitigate risk of a reaction. This communication between the eatery and the food allergic consumer is two-way. However, there are studies which show this communication is often suboptimal. Among 294 adults attending a FA conference in USA, 70% reported “always” alerting staff to their/their child’s, 14% do so using something in writing (83). This is particularly concerning as this group is likely more motivated than other groups. In a Dutch study of FA adults, 78% said they “always” alert restaurant staff of their allergy and 64% ask about ingredients in unlabelled products (85). These rates are even lower in studies of AARs within FE. A European study found 44% had informed staff (86) with similarly low numbers in two American studies which are twenty years apart: 55% (87) and 53% (88) gave prior notification to staff within FE. This topic will be explored in more detail in chapter 3. A qualitative study of adults with FA found that informing staff was not the norm but that conversations with staff about risk are more commonly initiated under circumstances of uncertainty, unfamiliarity and lack of knowledge and information (89). There is no data on difference in communication behaviours among food allergic consumers in the various different types of eateries.

(ii) Factors contributing to poor communication by food allergic consumer

There is data that there may be a reluctance to inform staff. Among nut allergic adults, checking the ingredients was a source of social embarrassment and the desire to avoid this sometimes led to increased risk taking (82). This is reiterated in another study which identified two major constraints to conversations with eatery staff were: being seen as ‘fussy’ or as a ‘nuisance’ (89). Some did not disclose their allergy to restaurant staff as they feared a conservative reaction that would further constrain food choices (82). Eating behaviour is strongly influenced by social context. We eat differently when we are with other people compared with when we eat alone. One reason for this is that conforming to the behaviour of others is adaptive and we find it rewarding (90). This may be particularly relevant for adolescents.

As well as that, a person’s ability to communicate may be a contributing factor. Numerous factors impact this e.g. personality, first language is not that of the FE staff. Language differences have been highlighted as a major barrier to confident communication about food content in food establishments both when trying to eat out in restaurants in foreign countries (as well as in ethnic

restaurants in the United Kingdom) (82). The parent's ability to appropriately communicate with eatery staff on their child's allergy is particularly important as their child matures and begins to model their behaviour. A UK qualitative study interviewed 15 parents of food allergic children ; they found parents attempt to equip children with self-assertion skills, so that they can effectively make others aware of their FA (61).

(iii) Communication by FE

As discussed, EU legislation from 2014 dictates that the presence of 14 allergens be disclosed in written information in non-packaged food. We know that consumers have a desire to receive both written and verbal allergen information in food establishments (91). A survey carried out by the FSAI in 2018 found that 3 out of 10 people find the allergen information that they have seen in FE as difficult to understand (66). Turner et al highlighted that food establishments can be fully compliant with current legislation, yet consumers may not feel confident that the FE can provide them with 'safe' food, for example, due to poor communication (92).

Food allergy knowledge /training among staff working in food establishments.

The literature reports a mixed level of understanding of FA among staff working in FE. An Irish survey carried out by the FSAI on Irish food businesses in 2019 found that allergens and ingredients labelling was the greatest food safety worry for Irish food businesses, with over half (53%) listing it as one of their top three concerns (93). It is important to point out that there is no obligation on food establishments in Ireland to have a specific policy around FA or to train their staff in FA.

Wham et al report a high level of confidence among restaurant and café managers in New Zealand in the preparation of an allergen free meal, however, less than a quarter had received any training on FA management (94) . The same study showed variation in practice among different types of venues, with restaurant managers more likely to have an emergency allergy plan than café managers ($P < 0.01$). Among 187 employees of eateries in Pennsylvania, only half said they were confident they could name all ingredients in the food they served (95); 10% considered removing the allergenic food from an already prepared meal would keep the FA customer safe. Parents themselves, also report difficulties relating to a lack of understanding of FA by eating out venues (64). There also appears to be inequities in the provision of allergen information for particular allergens in eateries. In particular milk allergy may be misunderstood. Adults wishing to avoid milk, reported that they felt less well-understood by restaurant staff which significantly limited their food choices (96).

Training on FA among staff in food establishments appears ad hoc. In one study, just over half of those working in eateries considered they receive adequate training on FA (95). Studies from the UK report rates of between 15-33% for FA training of staff working in food establishments (97, 98). Radke also highlights limited training in FA awareness for food service personnel and few restaurants with separate equipment or food preparation areas designated for allergen-free food (99). Not only is communication vital for the food allergic consumer but Endres makes the point, that it is also in the interest of food establishments to adhere to FA legislation; They highlight that the food industry has a ready opportunity to attract new consumers by moving beyond regulatory minimums through enhanced allergen communication efforts (100).

Focus on adolescents

There is a paucity of data on the participation of adolescents in social activities and visiting food establishments in particular. Socialising with friends whilst accepting the restrictions of allergen avoidance when eating out was felt to be particularly problematic for adolescents (61). Stewart et al found that adolescents with FA face many challenges including social isolation and resulting loneliness (101). Indeed, The European Academy of Allergy and Clinical Immunology's (EAACI) Task Force on Adolescents and Young Adults has recently emphasised the importance of supporting adolescents in getting involved in social activities (102).

2.2.4 Conclusion

The literature on disease specific QoL explore parent's thoughts and feelings around participation in social activity. However, there is an obvious gap in the literature on the actual participation of food allergic children in social activities and their visits to food establishments. It was with this gap in mind, as well as an awareness of the need to provide contextual information about the environment where accidental allergic reactions are occurring, we embarked on this part of the study. Irish society has changed significantly over the last generation. It remains unclear as to whether the Irish allergic population within this new society is restricted to a similar degree as US data (69, 70, 83) . Furthermore an in depth look at the Irish behaviour is more relevant to the wider western world now more than ever before.

Section 2.3 METHODS

Please refer to section 1.3 chapter 1 for the methods relevant to this chapter.

The participants were divided into 3 age groups: G1 (group 1, 2-4 years of age), G2 (group 2, 5-12 years of age) and G3 (group 3, 13-16 years of age).

The questionnaire described in section 1.3 (copy within Appendix) included questions about the child's participation in social activities e.g. attendance at parties, visiting friend's houses, going to discos, attendance at extracurricular activities outside of school, and camps during the school holidays. Visit to a friend's house was defined as visiting the house of a peer. Attendance at a party was defined as visiting a house/venue for a birthday party in association with other children. Information on participation in cultural holidays was collected also. "Trick or Treating" is a Halloween ritual custom where children in costumes travel from house to house, asking for treats with the phrase "Trick or treat". Typically, it is younger children that partake. The "treat" is traditionally peanut in the form of a "monkey nut" or confectionary. It is very popular in Ireland. Easter is another cultural holiday in Ireland. At Easter time, Irish children traditionally receive a chocolate egg from a folklore figure "the Easter Bunny". Eid al-Fitr is a religious holiday is celebrated by Muslims with consumption of many meals; it marks the end of the month-long dawn-to-sunset fasting of Ramadan. Other celebrations included wedding and First Holy Communion- a catholic celebration which typically involves a celebratory lunch.

Information was also collected on visits to food establishments. The term food establishments was used to describe all eateries: restaurants, hotels, pubs, cafes, fast-food establishments, takeaways. The type of food establishment was not defined for parents, but they were left to decide which term best described the FE they had visited.

Section 2.4: RESULTS

Chapter one describes the demographic data of the 531 children and adolescents enrolled into ReAACT and can be referred to when interpreting these findings.

Part A: Social activities

Participation in and food consumption at social activities

Parents were asked about their child's or adolescent's participation in a range of social activities. Overall, 83% of participants attended birthday parties. Of those in G2 (aged 5-12 years of age), 302 (97%) attended at least one birthday party annually; 103 (41%) of this group brought food from home to the parties. Parental supervision at parties reduced from 100% in those under 5 to 44% in G2. Overall, 387 (73%) go to a friend's house at least once a year with 239 (62%) eating food provided there (Table 2.4.1). A small number of adolescents attend parties (n=48, 66%), however the majority go to friend's houses (n=69, 94%). Over three quarters of participants in all age groups, have friends visit their house in preference to visiting a friend's house.

Table 2.4.1: Participation of food allergic children in social activities

| | Overall (2-16 years) N=531 | G1 (2-4 years) N= 141 (27%) | G2 (5-12 years) N=310 (58%) | G3 (13-16 years) N=80 (15%) |
|---|---|--|--|--|
| Parties n(%) | | | | |
| Attend parties | 439 (83) | 89 (65) | 302 (97) | 48 (60) |
| Bring own food to party* | 183 (41.5) | 44 (49) | 123 (41) | 16 (33) |
| Parents stay with child* | 225(51) | 89 (100) | 133 (44) | 3 (6.5) |
| Friends n(%) | | | | |
| Go to friend's house | 387 (73) | 46 (33) | 272 (85) | 69(94) |
| Eat food in friend's house** | 239 (62) | 30 (65) | 163 (60) | 46 (66) |
| Parents stay with child** | 88 (22.7)) | 46 (100) | 39 (14.3) | 3 (4.3) |
| Sleep over in friend's house | 57 (14.7)) | 0 | 32 (10) | 25 (36) |
| Discos /social n(%) | | | | |
| At least once in a year | 34 (6.4) | 0 | 20 (6.5) | 14 (18) |
| *Denominator: children who attend parties **Denominator: children who visit friend's houses Abbreviations: G1: group 1; G2: group 2;; G3: group 3 | | | | |

Those children who did not participate in social activities (birthday parties, visits to friend's house, discos/socials) (n=47), were more likely to be hen's egg allergic (RR 1.67, 95% CI 0.95 to 2.9; p=0.20) or have a previous history of anaphylaxis (RR 1.44, 95% CI 0.97 to 2.14; p=0.06) (Table 2.4.2). Proportionally more children in G1 were participating in social activities compared to G2 and G3 (p=.390), however 100% of this age group were supervised by parents during them. Of note, 8 of the 9 children with autism spectrum disorder (ASD) were participating in social activities.

Table 2.4.2: Clinical characteristics of food allergic children participating and not participating in social activities

| | Participate in at least one social activities * n=484 (91%) | Do not participate in social activities N=47 (9%) | RR (95% CI) | P value |
|---|--|--|---------------------|---------|
| Age group n(%) | | | | |
| Group 1 | 131 (27) | 10 (21) | 0.74 (0.38 to 1.46) | 0.39 |
| Group 2 | 281 (58) | 29 (62) | 1.14 (0.65 to 2.01) | 0.62 |
| Group 3 | 72 (15) | 8 (17) | 1.15 (0.56 to 2.38) | 0.39 |
| Ethnicity | | | | |
| White | 442 | 43 | 0.98 (0.36 -2.6) | 0.98 |
| Ethnic minority** | 42 | 4 | | |
| No. of food allergy n(%) | | | | |
| 1 | 158 (33) | 13 (27) | 1.24 (0.67- 2.29) | 0.48 |
| ≥ 2 | 326 (67) | 34 (73) | | |
| Type of allergy n(%) | | | | |
| Cow's milk | 83 (17) | 7 (15) | 0.85 (0.38 to 1.8) | 0.69 |
| Hen's egg | 226 (47) | 29 (62) | 1.67 (0.95 to 2.9) | 0.07 |
| Nut | 479 (99) | 46 (98) | 0.9 (0.41 to 2.5) | 0.48 |
| Previous anaphylaxis n(%) | 128 (26) | 18 (38.3) | 1.44 (0.97 to 2.14) | 0.06 |
| Abbreviations: | | | | |
| *Social activities= going to parties, friend's houses or discos/socials | | | | |
| ** Ethnic minority= Black/Black Irish and Asian/Asian Irish. | | | | |

Participation in extracurricular/ other activities outside of school

Overall, 375 (70%) of children participated in 1 or more extracurricular activities outside of school with a median frequency of once per week. Specifically, over 80% of children over 4 yrs do one or more extracurricular activities (Table 2.4.3).

Among children over 4 years who played sport, 57 (40%) travel to sports clubs to play matches in other clubs and 40 (80%) brought their own food with them. Of the 63 (86%) adolescents (G3) who took part in extracurricular activities outside of school, 21 (33%) play sport and 15 (71%) are

a member of a sports club; 8 (53%) of these travel with their team for an away match to another sports club.

Over a third of participants in G2 (n=115, 37%) and G3 (n=26, 33%), attend camps during school holidays. Amongst the children who attended school (G2 and G3), 339 (87%) go on school trips and 201 (59%) bring their own food on these.

Going to the cinema was another social activity that participants were asked about; 375 (75.3%) participants visit cinemas. Amongst the whole group, 197 (53%) eat food there and 176 (46.9%) bring their own food.

Parents were asked if their child had been on an overnight trip without their parents in the last year of which 10 adolescents (12%) had been. Of note no children in group 1 or 2 had travelled without their parents.

Table 2.4.3: Participation of food allergic children in extracurricular activities

| | All N=531 | G1 N=141 (27%) | G2 N=310 (58%) | G3 N=80 (15%) |
|--|----------------------|---------------------------|---------------------------|------------------------------|
| At least one activity n(%) | 375 (71) | 38 (27) | 256 (82) | 63 (72) |
| Any sport n(%) | 153 (29) | 12 (8.5) | 120 (39) | 21 (26) |
| Team sport n(%) | 142 (26) | 11 (8) | 114 (37) | 17 (21.25) |
| Swimming n(%) | 190 (35.8) | 10 (7) | 152(49) | 28 (35) |
| Other activity n(%) | 188 (35) | 13 (9) | 130 (42) | 45(56) |
| Sport: Gaelic football, hurling, soccer, rugby, basketball ,tennis, athletics); team sport: Gaelic football, hurling, soccer, rugby, basketball. Other activity: gymnastics, scouts, music, dancing, drama, art Abbreviations: G1: group 1; G2: group 2;; G3: group 3 | | | | |

Participation in cultural holidays

Halloween

A high number of children in both G1 and G2 participated in trick or treating (n=98, 70% and n=281, 91% respectively). Less than half of teenagers participated which is in keeping with their developmental stage.

Easter

In this study, 212 (40%) children received an easter egg, while 181 (34%) receiving a special “allergen-free” egg. 102 (19%) received another treat in place of a chocolate egg. Thirty-six (6.7%) of participants reported they didn’t celebrate Easter.

Christmas

Most families in this study celebrated Christmas (n=470, 89%). The majority of these families reported that they didn’t make any special changes to their behaviour at this time. Their risk

assessment continued regardless of the time of the year. Only 80 (15%) reported having to make more of an effort with the increased amount of confectionary at home.

Part B: Food establishments

Visiting food establishments

Overall, 523 (98.5%) children visit at least 1 type of food establishment (FE); restaurants were visited by 90% and fast-food eateries by 88%. Significantly fewer participants visited cafes (79%, 95% CI 73.3- 88.9, $p < .00001$) (Table 2.1). The median frequency of visiting a FE was once per month (lower quartile 1/3months, upper quartile 1/week).

Fewer participants in G2 (5-12 years) visited restaurants (87%, 95% CI 76.7- 97.7; $p = .269$) and cafes (74%, 95% CI 66.7 - 86, $p = .084$) compared to the other 2 age groups. The proportions eating in fast food eateries were similar across all 3 age groups (G1:90%, G2: 87%, G3: 91%).

Eating in food establishments

Overall, a quarter of participants (108, 23%) who visited restaurants brought their own food (Table 2.4.4). A larger number of G2 brought their own food to cafes ($n = 90$, 38%, 95% CI 30.6- 46.0, $p = .091$), with less in G1 (27%) and G3 (28%). Only 6% of participants reported bringing food to fast food eateries. There was a statistically significant difference in the number of children bringing their own food to cafes compared to restaurants (difference 11%, 95% CI 5.08-16.86, $p = 0.003$), restaurants compared to fast food eateries (difference 95% CI 11.9-20.6; $p < 0.05$) and cafes compared to fast-food eateries (difference 17%, 95% CI 12.65- 21.36, $P < 0.0001$). Almost half ($n = 262$) of participants did not restrict the kinds of FE visited and ate in all 3 types of FE. Adolescents were less likely to eat in all 3 FE (RR 1.1, 95% CI 0.8,1.3; $p = 0.36$). Almost three quarters of participants ($n = 389$) reported only eating in FE which were familiar to them. Half of adolescents ($n = 40$) visited FE without their parents.

Table 2.4.4 : Food allergic children visiting food establishments

| | Visit N(%) | Bring own food N(%) | Frequency of visits Median (UQ, LQ) |
|---|---------------|------------------------|--|
| Restaurant n (%) | | | |
| All | 479 (90) | 108 (23) | 1/mth (2/mth, 1/4mth) |
| G1 | 131 (95) | 30 (23) | |
| G2 | 279 (87) | 60 (22) | |
| G3 | 74 (93) | 18 (24) | |
| Café n(%) | | | |
| All | 418 (79) | 145 (34) | 1/mth (2/mth, 1/yr) |
| G1 | 118 (90) | 32 (27) | |
| G2 | 236 (74) | 90 (38) | |
| G3 | 64 (80) | 23 (28) | |
| Fast food n(%) | | | |
| All | 473 (88) | 30 (6) | 1/mth (2/mth, 1/2mth) |
| G1 | 123 (90) | 12 (10) | |
| G2 | 277 (87) | 18 (6) | |
| G3 | 73 (91) | 0 | |
| Take away n(%) | | | |
| All | 255 (50) | NA | 1/month (LQ 1 yr, UQ 1/wk) |
| G1 | | | |
| G2 | | | |
| G3 | | | |
| Abbreviations: FE: food establishment; G1: group 1; G2: group 2; G3: group 3, Yr:year, mth: month | | | |

A small number of participants (from G2 and G3) (26, 4.9%) did not visit or eat in any type of FE. These children were significantly more likely to be adolescents (RR 3.27, 95% CI 1.65-7.48, $p=0.0001$). They were also more likely to be nut allergic (RR 1.3, 95% CI 0.18-9.24, $P=0.79$) and have a previous history of anaphylaxis (RR 1.76, 95% CI 0.79 - 3.94, $P=0.163$) (Table 2.4.5).

Communication within food establishments

Of those that eat food served in FE, 405 (87%) always check the allergen information. Parents were asked what their course of action would be if the allergen information was not displayed: 248 (61%) would ask staff, 50 (12%) would order food that they believed should not contain allergens, 55 (14%) would not order any food and 53 (13%) would leave the eatery.

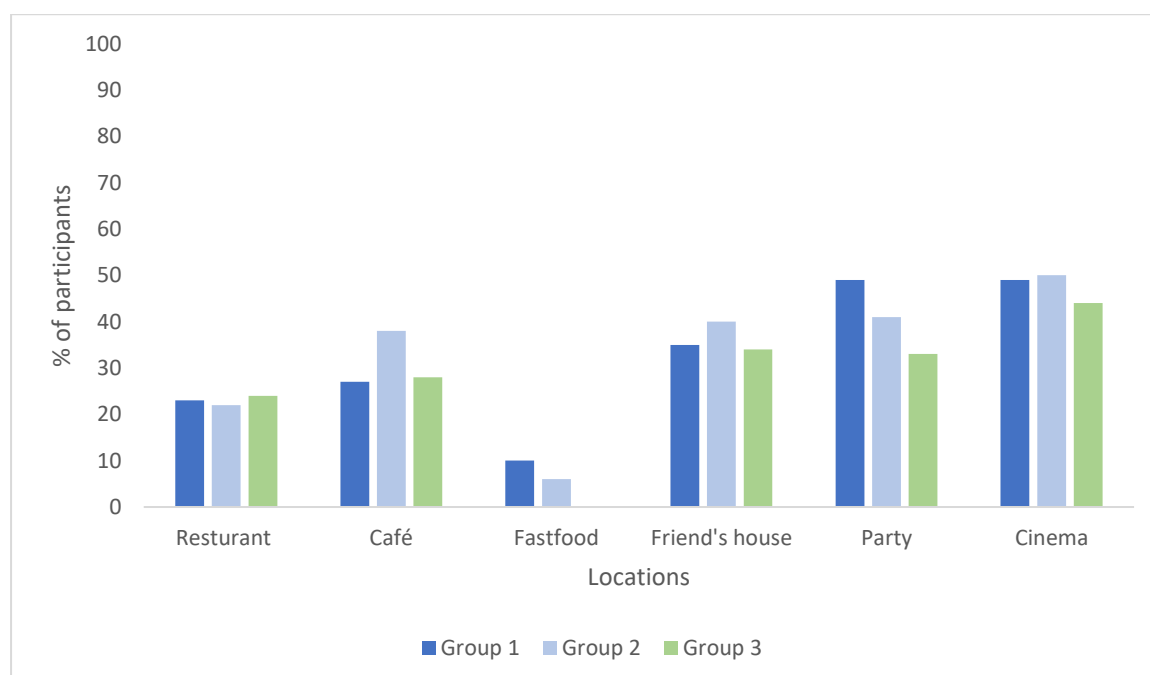
Among those who eat in FE, 338 (65%) always inform the server of their child's FA when ordering food, 105 (20%) sometimes do and 80 (15%) never do.

Table 2.4.5: Clinical characteristics of children eating versus not eating in food establishments

| | Eat food in at least one eatery N=505 (95%) | Do not visit/ eat in any FE N=26 (5%) | RR | 95% CI | P value |
|-----------------------------|--|--|------|-------------|--------------|
| Age group n(%) | | | | | |
| G1 | 141 (100) | 0 | | | |
| G2 | 294 (95) | 16 (5) | | | |
| G3 | 70 (88) | 10 (12) | 3.27 | 1.65-7.48 | 0.001 |
| Ethnicity n(%) | | | | | |
| White | 462 (95) | 23 (5) | | | |
| Ethnic minority* | 43 (93) | 3 (7) | 1.37 | 0.42-4.40 | 0.536 |
| Number of food allergy n(%) | | | | | |
| 1 | 169 (33) | 5 (19) | | | |
| ≥ 2 | 336 (67) | 21 (81) | 2.04 | 0.78 -5.33 | 0.142 |
| Type of allergy n(%) | | | | | |
| Cow's milk | 32 (12) | 1 (6) | | | |
| Hen's egg | 127 (48) | 13 (50) | 1.3 | 0.18-9.24 | 0.79 |
| Nut | 216 (83) | 26 (100) | | | |
| Previous anaphylaxis n(%) | 125 (25) | 9 (35) | 1.76 | 0.79 - 3.94 | 0.163 |

*Ethnic minority= Black/Black Irish and Asian/Asian Irish.

Figure 2.4.1: % of participants bringing their own food by age group



Legend figure 2.4.1: This displays the % of participants who brought food with them to both social events and FE. Cinema and parties had a larger proportion of children bringing their own food.

Section 2.5 : DISCUSSION

Appropriate social functioning is so important for the normal development and the progression of appropriate social skills. However as well as that, social activities have also been shown to be beneficial at improving the QoL of food allergic children; (81). This is the first large prospective study assessing both the participation of food allergic children and adolescents in social activities and their FE visiting habits in Ireland. Our data demonstrates that our food allergic patients are not over restricted and are “living with allergy”.

Social activities: attendance at parties

Birthday parties are an extremely important party of the social “calendar” for primary school children (5-12 years of age-G2). Non-peer reviewed Irish survey data indicates that (pre COVID) children under 8yr invited their entire school class to their party and that most primary school children on average received 8 to 12 invitations per yr (60). This implies that the Irish norm is for virtually all Irish children of primary school age to attend birthday parties. Therefore, the reporting by 97% of G2 parents that their child attends birthday parties is indicative of normal social practice amongst our allergic cohort and evidence of differential practices to FA families elsewhere. An American study (n=294, allergy clinic, unvalidated questionnaire) reported that 10% did not go to birthday parties because of FA (69). The reduction in the number of parents in our study accompanying their child at parties from 100% to 44% between G1 and G2 respectively, is also consistent with social norms and highly suggestive of parental confidence for their children in social circumstances. Similarly, adolescent informal attendance at friend’s homes, reported at 94%, contrasts with the traditional picture of social exclusion (18). The lower number of adolescents attending formal birthday parties is more likely due to their developmental stage, and that birthday parties are not as commonly arranged in teenagers. Across all age groups, we saw adaptation to FA being practiced while attending at parties and more informal gatherings in that 2/3 brought their own food. Our study was not designed to measure the quality of the experience and it is possible that it is impaired by FA. In the American study by Bollinger et al (mean age 5.1yrs) 70% of parents believed that their child’s FA significantly affected social activities such as birthday parties. This study also doesn’t tell us if these children brought their own food to these social events or ate the food provided. Preschool aged children would not have many opportunities to go to parties and therefore the fact that 65% of them attend parties is extremely reassuring. This age group are supervised by their parents which might explain their overall high levels of participation in social activities. They are products of an established allergy service whose parents have received advice and reassurance from the time of FA diagnosis. These findings

contrasts with older studies which found that parents of younger children report a more negative impact on social activities due to FA (71).

A recent study of HRQoL (which incorporated questioning on social functioning) in French children found it to be globally better in children with FA than in the general population which the authors state is due to recent improvements in FA management. However, only 54% of the study population carried AAIs at all times which might reflect a poor understanding of the potential risks of FA. A lower level of adrenaline carriage has been linked to underestimation of the severity of FA, which could modify HRQoL.

Participation in extracurricular activities

Over 80% of food allergic children in this study over 4-yrs, are participating in at least one extracurricular activity per week. (55). However, fewer food allergic children in this study are involved in a sport (39%) compared to reported norms 4,(57). There may be unidentified confounders that would explain this. Adolescent involvement in sports reflects common practice more closely (8).

Participation in cultural holidays

Cultural holidays are important social events with family and friends, all of which involve food. Halloween (an important tradition in Ireland) is always seen as a very frightening event for allergic children and their parents. It is reassuring to see that over three quarters of our children attending clinic, take part in “trick or treating”. There is little data of how many children overall actually go door to door on Halloween. The National Confectioners Association in the USA reported that 93 percent of children, teenagers, and young adults planned to go trick-or-treating or participating in other Halloween activities (103). Thus, the data from our study indicates some deviation from the norm. Christmas does not appear to be a challenge for food allergic families in Ireland with the majority of parents reporting they do not need to make any changes to their usual risk management strategies at this time of the year.

Visiting and eating within food establishments

There are no previous studies reporting the eating patterns of allergic children in specific types of eateries. The majority of children in this study are visiting FE. However, within that cohort the study revealed significant difference in behaviour with almost half of participants visiting and eating in all 3 types of FE while a further 1/4 are bringing their own food and thus, in essence, not getting the “eating out” experience. Participants in this study sought familiarity, with over three

quarters only eating in a FE that they had eaten in previously. This is echoed in the literature within many studies (7, 61, 82). This likely reflects a lack of confidence in FE and an unwillingness to trust them. Significantly fewer visited cafes and of those who did attend more brought their own food than to other types of eateries. which may be due to a perceived increased risk in cafes. The data shows that fast food restaurants are perceived as safer by parents who report being content to have their children eat the food prepared on site and for adolescents to visit unsupervised. Differences in perception of risk are further displayed by the evidence that more participants bring their own food to friends' houses and parties than to restaurants. This displays a belief that more control can be applied over food preparation in a restaurant than a domestic environment. Whether this is the case will be examined in future chapters

Communication within food establishments

Communication about FA within FE was suboptimal; checking of allergen information was less than 100% (87%) and only 65% informed restaurant staff of their child's FA. The literature reports similarly low levels of consumers informing FE of FA (48-78%) (83, 85-88). The underlying reasons for this poor communication could be many: a desire not to be seen as a "nuisance" (82, 89), poor communication/articulation skills (104), or indeed a belief that it is not necessary or ignorance of its importance. Consumers are responsible to advise FE of their food allergies and might view it as an opportunity to educate staff as well as teaching their food allergic child self-assertion skills (61). Ingredients often change in dishes, so it is important to ask about ingredients every time. Continuous communication between consumer and FEs is paramount to keep food allergic children safe in FE.

Non-participation in social activities or eating in food establishments

Although the majority of our cohort are "living with allergy", It is important to highlight there was a small number of children whose pattern of social functioning was restrictive. Overall, there were 47 (8.9%) participants who were not taking part in social activities. Although the numbers are small the data shows that that these participants were more likely to be hen's egg allergic or have a previous history of anaphylaxis. One might assume as hen's egg is contained in almost all-party cakes, and often in lightly cooked forms, this might be a deterrent from attendance at parties in particular.

There was also a small but notable number (4.9%) of participants who were not visiting or eating in any FE. These participants were more likely to be adolescents (RR 3.27, 95% CI 1.65-7.48,

p=0.0001), nut allergic (RR 1.3, 95% CI 0.18-9.24, P=0.79) and have a previous history of anaphylaxis (RR 1.76, 95% CI 0.79 - 3.94, P=0.163). The increased risk of restricted social activity and eating out with a history of anaphylaxis has been reported elsewhere. Mothers who have experienced anaphylaxis in their FA child are more likely to restrict a child's activities because of anxiety (105). Food allergic young adults who reported having experienced an anaphylactic reaction, reported more worry about their disease, and rated their parents as more overprotective than food allergic young adults who reported never having experienced anaphylaxis (106). Poor QoL, and a perception of isolation can manifest in parents, resulting in restrictions in their child, particularly if they have a negative perception on their management of the anaphylactic episode (107).

Adolescents

In this study, there was trend towards decreased participation among adolescents. A minority of adolescents (18%) attended discos and only 12% of adolescents went on an overnight trip without their parents. Less than half of adolescents ate in FE without their parents. Adolescents were over 3 times more likely not to eat in FE compared to the younger participants (p=0.0001). These figures are more likely to reflect avoidant behaviour than cultural norms; The Irish National Food Consumption Survey 2020 revealed that 20% of adolescents (13-18yrs) calories come from food prepared outside of the home (108). Learning how to travel with FA and eat in FE without parents is a learned skill, best learned prior to such time the child is independently living away from the family home. As discussed in chapter 1, adolescents in this study did not have an allergy service available to them at the time of their initial reactions/allergy diagnosis and therefore their parents may have used restrictive behaviour patterns as a means to avoid accidental reactions which they continue themselves into adolescence. This avoidant behaviour contrasts with the risk-taking behaviours in adolescents reported in other studies (109, 110).

The data we have collected provides data not been previously reported. It is imperative that we use the positive findings in this study to benefit the wide food allergic paediatric population both in Ireland and beyond.

Recommendations For now and for the future:

1. Encourage identification of food allergic children with restrictive patterns of socialisation as part of assessment by an allergy healthcare professional. Dahlsgaard point out that any restriction in developmentally appropriate activities is a good screen for anxiety (111).

2. Target adolescents. Group educational sessions with other food allergic adolescents with the allergy team could be an initial step in supporting this group.

3. Improve communication between food allergic consumer and food establishments. At the clinic, parents/children should be encouraged to question staff concerning the risk of allergens, and to carry translated information when travelling abroad. Communication aids such as role plays or the use of technology -enhanced simulation scenarios which allow parents or children to simulate an encounter with staff from a FE virtually may help to equip them with skills useful in these settings in real life.

Conclusion

Despite some challenges, the majority of our food allergic patients are taking part in age-appropriate social activities, attending FE and are thus can be said to be “living with allergy”. This reassures us, that the goal of our allergy clinic, to ensure that children with allergy are restricted as little as possible by their food allergies is being met. As allergists, we need to enquire about social functioning and educate our patients on how to communicate with FE. The information reported in this chapter is useful in its own right and will be used further in chapter 5 in the design of an educational tool. In addition, the understanding we have gained of the social and eating out practices of our population of food allergic children, gives us valuable environmental information which will provide context to the AARs occurring in this population (chapter 3).

Chapter 3: Accidental allergic reactions in Irish food allergic children

Section 3.1: INTRODUCTION

The current mainstay of FA management is avoidance of food allergens and the carrying of an anaphylaxis kit (emergency preparedness) (112).

Food allergic children and their families and other carers must always be prepared for the occurrence a severe, life-threatening reaction as accidental ingestion of allergens occurs despite avoidance measures. Furthermore, the likely severity of an accidental reaction is not predictable.

Accidental/unexpected reactions due to contact and/or ingestion can occur for a multiplicity of reasons. They can be due to food preparation related errors including intentional or nonintentional mislabelling of ingredients and accidental cross-contamination; failures of policy such as lack of education, planning and risk assessment; consumer/carer related factors such as failure to read ingredient lists, failure to consider the FA (human error)(85), lack of supervision and sometimes immunological factors such as cross reactivity (113).

In the examination of accidental medical incidents, it is important to be able to consistently define severity. In the case of hospital-based medication errors, scoring tools take into consideration whether the medication reached the patient, the potential risk to the patient and the actual risk (114). In the situation of accidental food allergic reactions, in almost all cases, the error is not identified until the food has been ingested and so scoring involves only the harm to the patient. As most accidental allergic reactions occur in the community, unlike medication errors, interpretation of the severity of the symptoms is more challenging. Currently there is no validated scoring system for classifying severity of food allergic reactions. World Allergy Organization (WAO) is planning the design and validation of an international definition and classification of severity for FA (115).

In the absence of such a scoring system, evaluating the severity of accidental food allergic reactions is not dissimilar to the challenge of defining the type of reaction and severity of vaccine reported reactions. Adverse reactions to vaccines are graded using the Brighton criteria. These are likely to exaggerate rates of severe reactions due to ascertainment bias (116). The Brighton criteria are not used in clinical allergy or in nonvaccine-related research settings to define anaphylaxis. Allergists in both clinical and research settings apply widely used clinical criteria for anaphylaxis such as the National Institute of Allergy and Infectious Disease (NIAID) Guideline 2005 which differs from the Brighton criteria in not containing levels of “diagnostic certainty”. The recent European guidance from the EAACI taskforce on anaphylaxis has highlighted the NIAID criteria as having high sensitivity (117).

A number of countries have reported their rate of AARs. However, this burden in Ireland has remained undefined to date. (This will be discussed in the following literature review). Comparison across jurisdictions can appear differential due to underlying study design variances. Errors are likely to exist in retrospective publications as parent's recollection of the details will fade. To ensure accuracy of data collected, studies should ideally be prospective, with data collected as soon as possible after the event. A Canadian study yielded an annual incidence rate of accidental exposure of 11.9% (16); parents were only contacted once a year and asked to recollect on any reactions. It is our unpublished experience from clinic, that recollection of small details fades within a matter of months, making diagnosis more difficult. This number contrasts with the prospective study by Clark et al who followed 785 patients with peanut and/ or tree nut allergy, in the UK and yielded an annual incidence rate of only 3% (13). These dramatically different figures are likely due to the differences in the environment within which they were collected rather than being incorrect.

Incidence of accidental reactions are not necessarily comparable across populations. They can be influenced by factors such as age, eating and social behaviours, local legislation. An understanding of environments and situations in which AAR occur within one's local environment can inform the development of local preventative strategies, legislation, educational targets.

Eigenmann et al, in an internet survey of food anaphylaxis, found that most reactions were facilitated by inadequate preventive measures (86). A number of studies have shown a decrease in AAR rate in those receiving education within the setting of the allergy clinic (11, 12). In our clinic, we provide all patients with specific education on allergen avoidance (discussed in detail in chapter 1 section 1.1). To be able to educate parents optimally, an understanding of behaviours and risks within our local society is required. This prospective study of AARs will allow us to gain insight into the frequency, severity, location and associated factors of accidental allergic reactions to food in Irish children.

Aim of this chapter:

To prospectively study the incidence and features of accidental allergic reactions in our population of food allergic children and adolescents attending an allergy clinic.

SECTION 3.2 : LITERATURE REVIEW

Introduction

The aim of this literature review is to summarise the existing literature regarding accidental allergic reaction in children to food, in particular, the frequency, severity and causes of such reactions.

The search was performed by one researcher in April 2019 and was repeated in April 2021. Seven electronic databases (CINAHL, Cochrane, EMBASE, Medline, Web of Science *Psychinfo and Scopus*) were searched to identify the studies. The snowball method was used , to screen the reference lists of full text papers and the author used her own judgement on whether to pursue these further. This is termed “backward snowballing” .

The following keywords were used based on disease characteristics (e.g. type of food allergy) and possible determinants (e.g. attitude, labelling, place of reaction and allergens): (food allergy) OR (food hypersensitivity) AND (reactions OR anaphylaxis OR anaphylactic OR accidental OR exposure OR milk OR egg OR OR fish OR peanut OR [sesame OR (sesame seeds)] OR [nuts OR almond OR hazelnut OR walnut OR (cashew nut) OR (pecan nut) OR [(brazil nut) OR (pistachio nut) OR. The limit title/abstract was used.

The articles were first screened for relevance to the stated study aims by reading the title and abstract. Of the articles that appeared to fit the criteria for the study after the primary review, the full text was then critically reviewed for relevance and quality.

The CoCoPop (condition, context, population) framework was used when assessing papers. This is described by Munn (118) and is a useful tool in reviewing epidemiological studies. Munn highlights that environmental factor can have a substantial impact on the prevalence or incidence of a condition so it is important that authors define the specific setting, and the population should be clearly defined and described in detail. As ReAACT collects a large body of data on the participants environment, we felt it was important to look for similar data in previous studies.

Data abstraction and synthesis: The included articles were analysed by one researcher. The characteristics of the studies were recorded in a Microsoft Excel sheet. The following information was documented: author, journal, and year; study design, participants and setting, FA definition and results relating to AARs (frequency of AARs, causes of AARs, severity of AARs), definition.

In studies with mixed populations (adults and children), results of children under 17 years were reported. The findings are reported by using a narrative summary technique. This is an overview of the available evidence addressing a research question or set of research questions related to a single topic, often produced within a short timeframe (119).

Results

There exists a reasonable body of literature on accidental allergic reactions (AARs) in children and adolescents. However, the studies themselves differ on many different levels and therefore it is difficult to make direct comparisons. Before describing the literature, I consider it is important to highlight these differences, so the reader is informed and has the ability to critically assimilate the information that follows.

Difficulties in comparing studies of allergic reactions:

1. Heterogenous groups of patients

The participants vary in their demographics e.g. their age, location, and type of allergen. They also vary in terms of their clinical characteristics. Some patients are recruited from allergy clinics, others through social media and others from food advocacy groups with the later more likely to be a more motivated group with respect to their FA (120) which may result in fewer AARs. Some studies only include studies where clinical care has been sought for the reaction.

Some patients may have a relatively new diagnosis of FA, others will be well established. Some may not have received education on avoidance of allergens and use of adrenaline autoinjectors (AAI), others will have received this education numerous times.

2. Food allergy definition is not consistent

Studies use different definitions for FA with the result that some studies may contain large numbers of participants that do not have a current allergy and thus not at risk of AARs. Relying on a history of a reaction in the distant past or evidence of sensitisation in young children as evidence of allergy is not a robust method to define current FA status (40). Oral food challenges (OFC) are the gold standard method to diagnose, however, it is not practical or feasible to do these on all participants in all FA studies to define allergy status. The majority of FA epidemiological studies in the past have relied on self-reporting of FA which is not as robust as a physician diagnosed FA. In the absence of the

resourcing to do OFCs, relying on a recent history of an allergic reaction with supportive allergy testing is the best marker for clinical allergy.

3. *AAR definition is not consistent*

There is a lack of consistency in the literature on the definition of an AAR . Some studies look at all (known and new) allergen reactions, other specifically look at known allergen reactions while others are not explicit. Other studies will exclude contact reactions (121).

This significantly hinders comparison of studies. In particular, a global consensus on anaphylaxis criteria is required (122).

4. *Data collection/methodology.*

The method of how, and by whom the data is collected differs considerably across studies. Whether the data was collected retrospectively or prospectively is important, with recall bias an issue in retrospective studies. The source of information of the AAR varies e.g. some studies rely on self-reporting by participants/parents . Others use medical records as their source document. Details of the AAR may have been transcribed originally by physicians or allergists from parents and others have a trained researcher collecting data directly from participants. Some studies use a proxy such as state claim's databases to collect data on AARs. Self-reported AARs collected by questionnaire are dependent on patients and carers understanding of allergy and perception of symptoms (122). A clinician collecting details of an AAR is more likely to identify relevant symptoms and correctly categorise the reaction. Furthermore, data is dynamic/ ever changing when collected in person which contrasts with the static nature of a questionnaire. A researcher collecting information verbally, can probe a participant for more information therefore increasing the likelihood of an accurate diagnosis of AAR compared with an online anonymous questionnaire.

5. *Severity grading differs among studies*

There is no universal consensus on how AARs should be graded with a number of grading systems in existence (123-125) all with their own merits. Dribin et al recently published a consensus severity grading system for acute allergic reactions developed using DELPHI methodology (126) with the aim to standardise the communication and

reporting of reactions among healthcare providers and patients. There are also different grading systems for anaphylaxis itself. There appears to be confusion around the grading of reactions e.g. one paper reports anaphylaxis grades but uses a general grading system for AARs (127).

6. *Time period over which AARs are collected.*

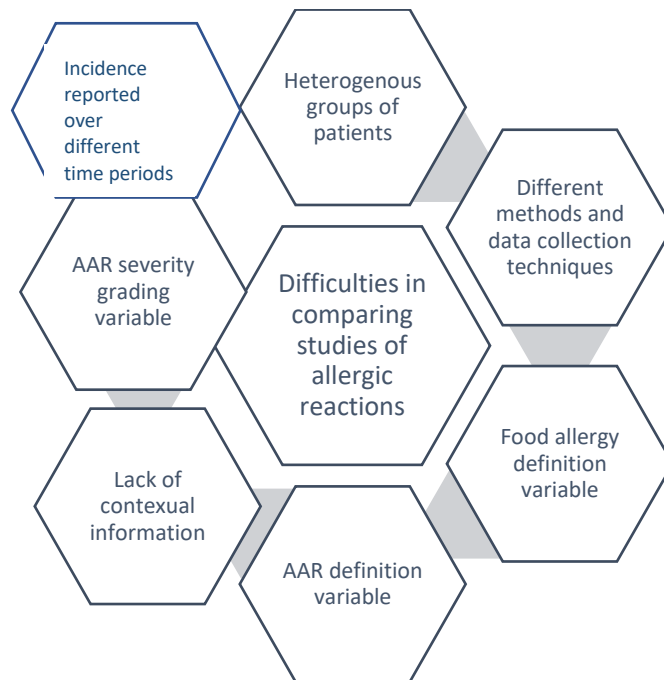
Some studies report an annualised AAR incidence(13, 128) and others report the incidence of “ever having” a reaction(129). . For those studies which examine the rate of “ever having” an AAR, the older the child is, the more time they have had for reactions to occur and therefore this will skew the results.

7. *Lack of contextual information*

To make sense of studies that report incidence/prevalence, it is necessary to know the context and environment where the data is collected. Most studies reporting AAR incidence give little information on this. Patient clinical characteristics are usually reported to give a sense of the level of atopy/ allergy in the individuals. However, there is usually no information regarding the behaviours of the population. For example, very few reactions occurring in eateries may not be indicative of good AAR prevention strategies but rather may reflect a paucity of visits to these establishments by food allergic individuals and families.

In summary, it is difficult to systematically amalgamate all of these studies for the reasons as highlighted above. Thus no metaanalysis of AARs has to date been published. One systematic review (130) of studies looking at AARs in those over 12 years is published. What follows is a descriptive narrative of the literature highlighting the main themes I have uncovered from my extensive review of the available literature.

Figure 3.2.1: Difficulties encountered when comparing the literature on allergic reactions



Overall incidence of accidental allergic reactions

There are no Irish studies looking at the rate of AAR in childhood or adolescence. The two most recent studies (published 2021) are from the USA (14, 120). Many of the studies looking at the frequency of AARs, study children exclusively with peanut or nut allergy.

Due to the heterogeneity of studies, as detailed above, there is a wide range of reported incidence rate reported for AARs in childhood. Furthermore, comparative studies have demonstrated that AAR incidence rate is specific to the environment where it is studied. In a multisite online survey of AARs, Hicks found that the rate of AARs was 27% lower in the USA compared to the UK ($p=0.0019$) (14) and Fierstein found the AAR rates were different within different regions in the USA- (Northeast versus West, OR: 0.71; CI: 0.53-0.94) (120). Table 3.2.1 illustrates the features of 25 of the studies reviewed.

1. All allergens

The annualised AAR rate varies among studies but is higher in studies of all allergens in comparison to studies of specific allergens e.g. peanut/treenut. A recent retrospective study of 2679 participants, (2510 <18) in USA from a patient registry found that just over 50% of participants reported at least one AAR in a year (120). The Australian Schoolnuts study which

looked specifically at 10-14 years old, reported an annualised incidence of 44.4%; (95% CI, 40.3% to 48.7%) (131). A study of infants reported an AAR rate of 0.81/year (132). Other studies report AAR rate of between 44% (133) and 58% (47).

2. *Peanut/treenut*

The annualised AAR rate for peanut (plus or minus treenut) ranges between 3 and 14.3% (16, 28, 48, 128) (Table 3.2.1). Clarke et al reported an annual incidence of 3% in their prospective study following 785 peanut allergic children who attended an allergy clinic in the UK in 2008 (48). In this study, preschool children had a lower number of reactions compared to school aged and none of their reactions were severe. Yu et al reported an annual incidence more than 4 times higher (14.3%) in their retrospective study of 437 children attending an allergy clinic in Canada in 2006 (17). Another Canadian paper looks at a larger cohort of 1941 peanut allergic children from allergy clinics and advocacy groups and reports an annualised rate of 12.4% (18). Other authors look at the incidence of peanut/treenut reactions over time periods that are either less than or more than a year which are difficult to compare with others. Sicherer did 2 retrospective studies (using a registry of patients) more than 20 years ago in the USA and reported rates of “ever” having an AAR in peanut/treenut allergic children: PN (48%); TN (34%) (27) and over a 5 year period : AAR to PN 55% and to TN 30% (134). Neumann-Shine suggests that the rate of AARs is decreasing. They report an annualised incidence of PN AARs as 4.7% in 2012 in their retrospectively collected data in USA. This is lower than previously collected data within the USA However, due to the difficulties stated above, we believe it is not possible to draw that conclusion from such heterogenous data. Another Canadian retrospective study showed similar annual AAR rates in 2012 (11.9%) and 2015 (12.4%) (18). This data suggests that although children are reacting to peanut and treenut, but not as frequently as other allergens. The annualised rate of severe reactions to peanut has been reported as 1.6% (15)

3. *Cow's milk and Hen's egg allergy*

Many studies suggest an allergy to cow's milk or hen's egg is a risk factor for accidental allergic reactions. Fierstein et al found respondents with egg (OR: 1.71; CI: 1.37-2.14) or milk (OR: 1.95; CI: 1.56-2.44) allergy were significantly more likely to report having 1 or more reactions per year, in comparison with patients with other types of food allergies. This is likely due to the fact they are present in a multitude of foods. In one study, egg and milk allergic infants had a median of 2 reactions over 16 months (135). Hicks reported that 91% of children (median 7 years) had an AAR to cow's milk since diagnosis (14). In a small Japanese retrospective questionnaire study, eggs (44.1%) and milk (35.1%) were the most common causes of AARs (136). A retrospective

study of 88 Spanish children reported an annualised AAR rate in milk allergic children of 40% (137); 8/53 (15%) were severe. The same author reports an annualised AAR rate to hen's egg among 92 egg allergic children of 21% (138). These are small studies, but they do show that children with cow's milk and hen's egg allergy frequently encounter these allergens.

4. Unknown allergens

Studies show that the allergen causing a reaction may not be clearly identifiable. Fierstein found in 16.6% of AAR the causative allergen was not evident (120). Another retrospective study of members of a FA charity showed that in a third of reactions the allergen may not be identified by parents, however most of these reactions were in adults (139).

Incidence of anaphylaxis

The annualised rate of severe reactions ranges across studies and is reported in different ways. A systematic review of paediatric food anaphylaxis in the general population reported an incidence of 1 to 77 per 100 000 person-years (140).

It is reported that most cases of anaphylaxis occur when the child is supervised by an adult (31%) and in most cases the parent (141). This is likely because children are most commonly served food by a "supervising" adult which is most often the parent. The implicated allergen varies among studies; with both milk and egg (142) and peanut/treenuts (143) implicated as the commonest trigger. In one study, 85% of severe reactions had co-existing asthma (139). In a small study of milk reactions, the frequency of anaphylaxis to milk was 10-fold higher in asthmatic children (odds ratio, 10.2; 95% CI, 1.13-91.54) (144). As well as being an overall risk factor for AARs, it is well established that adolescence is a risk factor for severe AARs (OR 1.65 (95%CI 1.41-1.93) (145) with the median age for severe peanut reactions as 13 years in one study.

Table 3.2.1: Previous studies reporting incidence of accidental allergic reactions.

| | Study authors | year | Country | Allergen | Design | Participants | Data collection | Frequency of AARs |
|----|---------------|------|-------------|----------------|-----------------|---|---------------------------|--|
| 1 | Cherkaoui | 2015 | Canada | Peanut | Retro and prosp | Allergy clinic/ advocacy groups N=1941 | Mailed Qn (self-reported) | Annualised incidence 12.4% (95% CI, 11.4, 13.4). |
| 2 | Yu | 2006 | Canada | Peanut | Retro | Allergy clinic N=437 | Online Qn (self reported) | Annualised incidence 14.3% (95% CI, 10.0% to 19.9%) |
| 3 | Uguz/ JOB | 2005 | UK | All | prosp | Advocacy group N=109 (75 Children) | Online Qn (self reported) | 126 AR over 6 months (89% food) |
| 4 | Clark | 2008 | UK | Peanut/treenut | prosp | Allergy clinic N= 785 | Not described | 3% annual incidence rate |
| 5 | Mc Williams | 2017 | Australia | All | Retro | School students 10-14yr | Self reported | Annualised incidence 44.4%; (95% CI, 40.3% to 48.7%) |
| 6 | Eigenmann | 2002 | Switzerland | All | retro | N=61 (60% under 16) | Online Qn (self reported) | |
| 7 | Yanagida | 2019 | Japan | All | retro | N= 45,806 Children attending preschool | Postal survey | 3497 (7.6%) AAR among food allergic children in last year in preschools |
| 8 | Fleisher | 2012 | USA | All | Prosp | Allergy clinics N= 512 | Qn in person | annualized incidence rate 0.81 (95% CI: 0.76–0.85) (preschool aged children) |
| 9 | Sicherer | 2001 | USA | Peanut/treenut | Retro | Patient registry N=4586 | Phone Qn | In, School/childcare 16% ever had AAR |
| 10 | Nguyen-Luu | 2012 | Canada | Peanut | Retro | Allergy clinic N=1411 | Mailed Qn (self reported) | Annualised incidence 11.9% (95% CI, 10.6–13.5) |
| 11 | Sicherer | 2004 | USA | Seafood | Retro | | Phone Qn | Ever had AAR 58% report >1 AAR (fish 58%, shellfish 57%) |
| 12 | Ewan | 2001 | UK | Peanut/treenut | Retro | Allergy clinic N=567 | Allergy physicians | 15% AAR over mean 21 months |

| | | | | | | | | |
|------|-----------------|------|----------------------|----------------|---------|---|---------------------------|---|
| 13 | Shah | 2009 | | All | Retro | | Qn (self reported) | 44% AAR incidence rate (timeframe not specified) |
| 14 | Fiersten | 2021 | USA | All | Retro | Patient registry N=2679 (169 >18yr) | Online Qn (self reported) | Annualised reaction incidence 37.7% >1 AAR 12.8% 1 AAR |
| 15 | Boyano-Martínez | 2012 | Spain | Egg | Retro | Allergy clinic N=92 | In person Qn | Annualised reaction incidence 21% |
| 16 | Boyano-Martínez | 2009 | Spain | Milk | Retro | Allergy clinic N= | Check | Annualised reaction incidence 40% |
| 17 | Neuman-Sunshine | 2012 | USA | Peanut | Retro | Allergy clinic N=782 | Check | AAR 4.7% per year (30.9% over 5.3 yr) |
| 1118 | Clarke and Ewan | 2005 | Uk | Peanut/treenut | Prosp ? | Allergy clinic N=615 | Check | 21% had AAR (median 39 month follow up) |
| 19 | Sicherer | 2001 | USA | Peanut/treenut | Retro | Patient registry N=5149 | Allergy physician | Ever had AAR (?timeframe) PN (48%); TN (34%) |
| 20 | Sicherer | 1998 | USA | Peanut/treenut | Retro | Allergy clinic N=122 | | Over 5 years: AAR to PN 55% AAR to TN 30% |
| 21 | Kansen | 2020 | Holland | Peanut | Retro | Allergy clinic post DBPCFC N=41 | QN Self reported | Over 3 years: 41% had AAR |
| 22 | Nowak-Wegrzyn | 2001 | USA | All | Retro | Allergy clinic N=132 | Phone qn (self reported) | Over 2 years: 58% reported AAR |
| 23 | Furlong | 2001 | USA | Peanut/treenut | retro | Patient registry N=129 | Phone qn (self reported) | Over 1 year: 13.7% of all AARs occurred in eatery |
| 24 | Oriel | 2021 | USA | All | Retro | Patient registry N=1579 (<18) | Qn (self reported) | 21% of all AARs occurred while dining out |
| 25 | Hicks | 2021 | Multi site (USA, UK) | All | Retro | Online/allergy clinic/registry N=558 | Online Qn (self reported) | Annualised AAR incidence Adolescents 0.21 Children 0.53 |

Abbreviations: AAR: accidental allergic reactions; QN: questionnaire; Pros: prospective; retro: retrospective;

Location of accidental allergic reactions

There are a number of locations where AARs can occur. Reactions occurring in schools and in preschool childcare services are described in chapter 4. Home and food establishments are focused on here as they are frequently reported as sites of AARs.

Home

Almost all studies report the largest proportion of AARs occurring at home (ranging from 25 to 54%) (18),(128) (13, 139), (131) (86), (146) (14) (136) (120, 147). Interestingly, even in the teenage cohort home remains a high-risk environment for AARs. In Schoolnuts, 45% of AARs among 10-14 yr. olds occurred at home (131). However, the study doesn't define how many or how often participants eat outside the home. This is universal throughout studies on AARs, where the eating habits of participants are not reported. It is difficult to come to any meaningful conclusions without this data. Most cases of anaphylaxis also occur at home (42%) (141) and (58%) (127).

Food establishments

In previous studies, food establishments (FE)(inclusive of restaurants, fast food outlets, cafes, takeaways) are the locations for a number of reactions (12-21%) (88, 121, 136, 147). The 2 largest studies on the topic come from the USA and were performed 20 years apart: Furlong in 2001 (87) and Oriel in 2021 (88). Both populations are taken from registries which self-report their AARs and food allergies, thus the potential for over reporting. It is important to note when reviewing studies reporting reactions in food establishments, that some only report restaurant AARs (or define restaurants as all eateries) and others report the number of reactions in all types of food establishments type of eatery. Oriel et al found that most reactions occurring in FE are in cafés and fast-food outlets (88). Amongst all FE, peanut (20%), treenut (17%) and milk (19%) were the main implicated allergens (88). In this study and in the older study by Furlong et al (87),over a quarter of reactions were severe (27% and 28% respectively) (87, 88). Another American study found that poor communication with waiting staff ((12.0%; CI: 10.5%-13.8%) and a poorly written or unavailable allergen list (18.6%; CI: 16.3%-21.1%) were features of AARs in eateries (120). However, a considerable number of reactions (12-55%) occur even after the restaurant staff (most commonly the waiter), have been informed of the child's allergy (87, 88, 120). Also of concern, Oriel reported that 13% of reactions occur after both the

waiting staff have been informed and the menu containing allergen information have been checked (88).

Allergen administration

Parents administer the allergen containing food in a large number of the reactions (36-64%) (13, 135) with self-administration of the allergen being the next most common (13). In younger children, food is given by a non-parent in half of reactions (50.6%) (132).

Allergen exposure

AARs occur most commonly after ingestion of the offending allergen but can also occur when there is contact with the allergen. Boyano et al found 17% of egg allergic reactions were due to contact and all were mild (urticaria) (121). Previous studies of peanut and treenut have highlighted that contact reactions are also mild (13);

Causes of accidental allergic reactions

The causes of reactions are multifactorial; It can be difficult to determine one cause of a reaction. This will be explored in more details within the discussion. In addition, there is no universal definition for “accidental” in the context of food reactions. Two studies used the term “purely accidental” to describe the cause of reactions: 46% (136) and 61% (14). Fleischer et al attempt a more detailed description of “purely accidental” to mean forgetfulness, lack of supervision, not checking a label on product etc. In their study of preschool aged children, 64% or reaction were categorised as purely accidental. (148). Cross contamination was considered the cause of reactions among a large number of patients (24.1% (CI 21.9-26.3)recruited from an American patient registry (120). In another retrospective study, 70% of reactions to pre-packaged food occurred when the label was not read (14). 83% of reactions to milk were foods that were prepacked .

The most comprehensive data on causes of AARs comes from two Dutch studies from the same research group involving adults only, however they are discussed here as they give an insight into behaviour. The first is of 153 reactions among 73 adults found that ingredients were not checked in 31% of cases; in another 37%, the suspected allergen was not listed as an ingredient or in a warning on the label (85). The 2nd study, analysed culprit foods causing the AARs and found 37% of foods had 1-4 undeclared allergens with milk posing the highest risk (149). Bread, cookies,

chocolate, and meat were implicated in 53% of foods with undeclared allergens. A Swedish study also highlighted milk as being the most commonly undeclared food allergen causing unexpected allergic reactions in (150).

Management of accidental allergic reactions

Few allergic reactions require medical treatment in an emergency department of a hospital. Most studies report the majority of participants as managing their reactions at home with antihistamine home (16). Capucilli et al extrapolated that the 4-year incidence of AARs requiring ED attendance was 0.49% (95% CI, 0.39-0.6%) in their retrospective chart review (151). Even fewer children need to be admitted to hospital after a reaction.

Universally, there is a low rate of intramuscular (IM) adrenaline use for anaphylaxis. Rate of adrenaline use for severe reactions range from 0% among 41 children attending a Dutch allergy clinic (152) to 39% (120) with most studies reporting rates between 11-30% (14-16, 18, 131, 132, 139). Other types of medications are administered in the setting of ED before adrenaline e.g. antihistamines (77.5%), oral corticosteroids (85.7%) (153). Delayed adrenaline use is associated with fatal anaphylaxis but not always; in one study, a third of fatal cases, adrenaline was given promptly (154).

Risk factors for accidental allergic reactions

A number of studies have reported that those with multiple food allergies are at greater risk of AARs than those with one at risk (aOR, 1.9 [95% CI, 1.1-3.1] (131). Two studies looking at preschool aged children found increased AARs associated with increasing number of allergies ($P < 0.0001$) (132, 155). Kapoor et al report an annualised AAR rate of 0.2 in children with 1 FA, 0.7 reactions per year in children with 2 FA and 3.4 reactions per year in children with 3 or more FA (12). A current diagnosis of asthma is a risk factor for more reactions to (i) all allergens (OR 1.7 [95% CI, 1.1-2.6]) (131) and to (ii) peanut (OR[95% CI]=1.33[1.18-1.51]) (145). The age of the child likely plays a role, however there is conflicting evidence among studies. Very young children appear to have more AARs (155). Adolescents with peanut allergy have more AARs compared to younger children : OR, 2.33; 95% CI, 1.20–4.53 (16). As previously mentioned, the SchoolNuts Australian cohort found that adolescents are frequently exposed to allergens (annualised AAR rate of 44.4%) (131). However, another study found the annualised rate of AARs was significantly lower in the adolescent population at 0.21 vs 0.53 in children ($p < 0.0001$) (14).

Accidental allergic reaction while on vacation

Vacations are an important part of family life. However, there is very little literature available on AARs whilst on holidays. Nine studies were found, however much of the data pertains to adults, is related to airplane travel and almost all studies look specifically at peanut and tree nut allergy and are from the USA. As such, there is a paucity of information for the milk or egg allergic child going on holidays.

There is a lack of data on all cause reactions in children that occur whilst on holidays, representing a significant gap in the literature. A proportion of reactions occurring within FE in the above studies may have occurred on vacation (where many meals are not self-prepared) but this not highlighted in the particular studies. The overall incidence of AARs among nut allergic adults/children whilst on airplanes is high 9 (156)-19.7% (157). However a relatively low number of these reactions are due to ingestion 13% (157), 33% (156) with the majority described by participants as being due to inhalation despite there being no evidence that inhalation of nut particles in the air can propagate an AAR. There is a low level of adrenaline use on flights (13.3%-33%, 10% Greenhawt 2009). Most reactions (69%) among nut allergic individuals are due to peanut (157). A qualitative study from the UK highlights strategies that nut allergic adults use whilst travelling abroad e.g. only visiting English speaking destinations and eat very plain food (158). Leonard et al found that 90% will not leave the USA and half only eat meals in their room (159).

Conclusion

There is no data on the incidence of AARs in the Irish setting. There is a large range of incidences reported in other countries. While accepting the limitations discussed, this highlights those figures cannot always be applied to different environments. Much of the data on incidence in children pertains to nut reactions, however, cow's milk and hen's egg are common allergens with cow's milk cited as the commonest cause of anaphylaxis. Therefore more data on all cause AAR in childhood is warranted. The commonest location for reactions is in the child's home. But the studies in the literature fail to report contextual data so we do not know if reactions are more common because children do not /rarely eat in other locations. We have already reported this contextual data in chapter 2. There also appears to be conflicting evidence with regards adolescents with some studies reporting they are more at risk of AARs with other suggesting they

are not. I have also found there is a significant lack of information on FA in children and going on holidays. Therefore a prospective study is required for Ireland to gain insight in to and optimise strategies for the prevention of avoidable reactions.

Section 3.3 METHODS

Introduction

The main methods of this study have been described in chapter 2 (section 2.3) . The following is a description of the specific methodology used in collecting the accidental allergic reaction (AAR) data.

Participant selection and recruitment

Children with a defined FA between 2 and 16 years were recruited. The inclusion criteria and how the participants were defined as food allergic has been discussed in section 1.2 (Chapter 1).

Data Collection

AAR data were collected prospectively for 12 consecutive months, on all participants recruited between November 2018 and May 2019. Collection of data on AARs was completed by May 2020. A proportion of participants were still being followed at the onset of the first wave of the COVID-19 pandemic and the associated lockdown that was imposed. In Ireland all schools and preschool CCS were closed from 13th March 2021. All social gatherings were banned from March 24th with food establishments only operating take away from that date (25, 26). Participants who had ended their 1-year follow-up on or before 12th March 2020 were deemed to have been followed during “normal circumstances”.

All participants were contacted at 3 monthly intervals from the time of recruitment. All follow up calls were made by phone by a single researcher. Three attempts were made at each time-point to contact participants. In some cases, participants contacted the research or clinical team to report a reaction, prior to the researcher contacting them.

A questionnaire (copy in Appendix) was used by the researcher to record details of the reported reaction, from the parent, over the phone; Details recorded included: date, time of day, symptoms, timing of onset of symptoms, trigger allergen, route of exposure, circumstances of exposure, history of activities prior to the reaction, location, on holidays, presence of animals. A detailed response to the exposure which included medication use, medical attention, healthcare professionals involved, and outcome was also recorded.

Definition of an accidental allergic exposure:

Accidental exposure was defined as an unexpected or unplanned exposure (contact or ingestion) to a food allergen, in a child practicing avoidance measure, resulting in IgE mediated symptoms. A non-accidental (or purposeful) exposure was defined as exposure where the allergen was deliberately given to the participant either because a reaction was not expected or was anticipated as part of medically supervised, home based, tolerance promoting programs using either the iMAP Milk Ladder or the IFAN Egg Ladder. Reactions during hospital based oral food challenges were also excluded.

Reactions that were suggestive of pollen food syndrome (PFS) were also collected and included if avoidance was being practiced.

Criteria used to determine whether a reaction was an IgE mediated accidental allergic reaction included: time kinetics (interval between eating food and symptoms- within 2 hours); type of symptoms and response to treatment, previous history of reactions to index allergen. A convincing clinical history required clear evidence of food having been eaten or contacted with in the previous 2 hours.

Symptoms considered in close association with eating included sudden onset of rash and erythema, pruritic rash, urticarial eruptions, angioedema, new onset rhinorrhoea, nasal congestion, persistent sneezing, ocular itch, ocular redness, oral tingling, oral itch, sense of throat closing, tongue swelling, hoarseness, drooling, abdominal pain, nausea, vomiting, sudden cough, wheeze, noisy breathing, difficulty breathing, weakness, dizziness, pallor.

We defined urticaria/angioedema that occurred on contact with a known allergen for that child as a “contact” reaction. Children with a known exposure to an allergen that they have been defined as allergic to and subsequently display immediate skin symptoms on contact most likely are having an immediate/IgE type reaction. This is almost certainly true for those children outside of infancy. These contact reactions in very rare circumstances progress to systemic symptoms (belen et al). Unintentional transfer to the mouth could potentially cause anaphylaxis in severely allergic children. As such is it important to study these kind of reactions.

The details of all reactions were recorded over the phone or in person with one of the carers so that the researcher had the opportunity to question the reporter in detail and clarify patient’s

understanding certain terms such as of wheeze, “tongue swelling”, “throat closing” etc. This strengthened both the diagnosis and the grading of the AARs.

Potential other causes of symptoms were considered as part of each reaction analysis including insect sting, idiopathic urticaria, allergic rhinitis, contact dermatitis to lotions etc.

Definition of the trigger of the allergic reaction.

The trigger of the AAR was either “identified” or “unknown”. This identification was left to the interpretation of the individual researcher as a result of careful history taking along with referring to cases notes and previous allergy testing (SPT, IgE and OFC).

The following steps were taken to identify the allergen:

1. Parent was asked what steps they had taken to identify the allergen
2. If parent was unable to identify the allergen, an attempt was made to identify it with them, by looking online.
3. If this was unsuccessful, parents were asked to retrieve the food label and send it to the research team.
4. For reactions in food establishments where the parent was not sure of the allergen, they were instructed to review the food ingredients with staff there.

Grading the reactions:

We graded the reactions as either anaphylaxis or non-anaphylactic allergic reactions. The (National Institute of Allergy and Infectious Disease (NIAID) 2005) (123)clinical criteria for anaphylaxis were used to define anaphylaxis (Table 3.3.1).

Table 3.3.1 National Institute of Allergy and Infectious Disease grading of anaphylaxis

| |
|--|
| Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled: |
| Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, pruritus or flushing, swollen lips-tongue-uvula) |
| AND AT LEAST ONE OF THE FOLLOWING: |
| a. Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia) |
| b. Reduced BP or associated symptoms of end-organ dysfunction (e.g. hypotonia [collapse], syncope, incontinence) |
| 2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): |
| a. Involvement of the skin-mucosal tissue (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula) |
| b. Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia) |
| c. Reduced BP or associated symptoms (e.g. hypotonia [collapse], syncope, incontinence) d. Persistent gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting) |
| 3. Reduced BP after exposure to known allergen for that patient (minutes to several hours): |
| a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP* |
| b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline. |
| PEF, Peak expiratory flow; BP, blood pressure. *Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year, less than (70 mm Hg 1 [2 3 age]) from 1 to 10 years, and less than 90 mm Hg from 11 to 17 years. |

Taken from: Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Jr., Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol.* 2006;117(2):391-7.

The AARs were graded by one researcher. If there was an ambiguity, the reactions were discussed with the other member of the research team and a decision was made. As symptoms

were elicited verbally directly from the patients within 3 months of the reaction occurring, details could be clarified in real time ensuring the classification of the reactions was accurate.

Aftercare of participants who experienced an anaphylactic reaction.

In the case of a severe/ anaphylactic reaction: participants were invited back to clinic within 6 weeks for an evaluation with their consultant. This is standard procedure in the clinic also in non-study patients. Similarly, any patient that had adrenaline delivery was invited back for urgent review. If a patient had 3 notifications of reactions during the study the consultant/PI will also be informed.

Cause of reactions

The following questions were asked to of the parent to determine contributors of causation:

1. Who was present?
2. Who gave the child the food?
3. Were the ingredients checked?
4. Circumstances of the reaction?
5. Any other information.

Special occasions or celebrations.

A recording was made as to whether the reaction had occurred as part of a special occasion or celebration such as a birthday, Halloween, or a religious festival such as Christmas, Easter, First Communion or Eid al -Fitr.

Statistical methods

Descriptive statistics were compiled for all variables using SPSS version 27 (2020; SPSS Inc., Chicago, IL, USA). The annual incidence rate of AARs was expressed as the number of events divided by the sum of the patients at risk. Not all participants had a full 12 months of data collected. The AAR rate was calculated for all participants (irrespective of follow up length) and also for those with a full 12 months of follow-up. By doing this, any potential bias resulting from variable lengths of observation on the estimate of the rate of AARs was reduced.

Allergic reaction (yes or no) is a binary categorical variable. Chi-square test or exact test was used to examine the association of allergic reactions with different parameters. Continuous

variables were compared using two-sample t-tests and were visually assessed for normality using histograms. All tests were two-sided. Relative risks were calculated. Confidence intervals were set at 95% and a p value of ≤ 0.05 was taken as significant.

Section 3.4: RESULTS

Overall incidence of accidental allergic reactions

A total of 220 food related allergic reactions were recorded among 498 participants, yielding an overall annual incidence rate of 0.44 (95% CI, 0.38-0.50). This was among participants with partial and full 12 month follow up data. More than 1 reaction was reported by 39 participants (25%). 441 participants had a full 12 months data (contact was successful every 3 months). The annual incidence in these 441 participants was similar at 0.45 (95% CI 0.39- 0.52). In addition, the annual incidence in participants who had 12 months follow-up during normal circumstances (pre-pandemic related lockdown) was 0.42 (95% 0.34- 0.49).

There were significantly less reactions reported at the final 12 month follow up call (last quarter) (n=40) compared to the first quarter (n=70) ($p < .0099$). There were 53 reactions in the 2nd quarter which was not significantly different to the last quarter ($p < .27673$). Finally there were 57 reactions in the 3rd quarter of follow up.

The second and third quarters had similar numbers of AARs recorded (n=53, n=57 respectively).

Of the 498 children with follow up data, 155 (31.1%) reported at least 1 AAR over the one-year study period. The calculated mean number of AARs per child was 1.2 (SD 0.52). Of the 57 participants with less than 12 months follow up, the mean follow up was 9 months. Of note, 19 participants were uncontactable at the end of their 4th quarter (12 months timepoint) by phone. This coincided with the beginning of the Covid-19 pandemic. All of these participants were contacted subsequently between 6-9 months later to check for AARs that occurred during their last quarter in the study.

Reactions were graded as anaphylaxis (n=31, 14.1%) or non-anaphylaxis (n=189, 85.1%). 31 cases of anaphylaxis occurred in 29 children. The incidence of anaphylaxis calculated was 0.062 (95% CI 0.042- 0.088) and the incidence of receiving adrenaline was 0.024 (95% CI 0.012-0.042) (Table 3.4.2).

The clinical characteristics of the participants who had reactions were not significantly different to those who did not react (Table 3.4.1).

Table 3.4.1 Clinical characteristics of children with accidental allergic reactions

| | Participants reporting reactions N=155 (31%) | Participants reporting no reactions N=343 (69%) |
|---|---|--|
| Gender n (%) | | |
| Male | 103 (66.5) | 232 (67.6) |
| Female | 52 (33.5) | 111 (32.4) |
| Median age at recruitment (years) (Lower quartile, upper quartile) (years) | 7 (4,10) | 7 (4, 10) |
| Group 1: 2-4 years n (%) | 46 (29.7) | 85 (24.8) |
| Group 2: 5-12 years n (%) | 89 (57.4) | 202 (58.9) |
| Group 3 : 13-16 n (%) | 20 (12.9) | 56 (16.3) |
| Ethnicity n (%) | | |
| Irish Celtic | 129 (83.2) | 286 (83.4) |
| Caucasian non-Irish | 10 (6.6) | 29 (8.5) |
| Afro Caribbean | 5 (3.2) | 4 (1.1) |
| Asian | 11 (7) | 24 (7) |
| Number of food allergies n (%) | | |
| 1 food allergy | 56 (36) | 110 (32.1) |
| ≥ 2 food allergies | 99 (64) | 233 (67.9) |
| Specific food allergies n (%) | | |
| Cow's milk | 27 (17) | 50 (14.5) |
| Hen's Egg | 60 (38) | 122 (35) |
| Peanut | 92 (58) | 223 (65) |
| Treenut | 77 (50) | 171 (50) |
| Fish | 14 (9) | 26 (7.5) |
| Previous history of anaphylaxis n (%) | 41 (26) | 94 (27) |
| Emergency accommodation at any time during the study n | 0 | 0 |

Incidence of accidental allergic reactions by age group

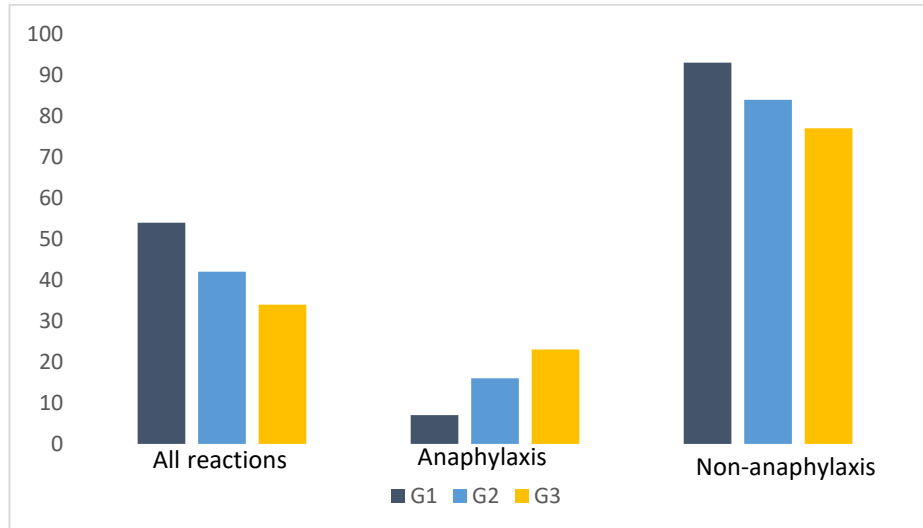
The breakdown of the reactions by age groups was as follows: G1=71 (32%), G2=123 (56%), G3=26 (12%). The annual incidence of reactions in G1 was significantly higher compared to G2 and G3 (RR 1.4, 95% CI 1.14-1.71, p=0.001). There was a lower number of reactions in G3 compared to those under 13 (p=0.155). Of those who reacted, G3 (adolescents) were twice as likely to have anaphylaxis compared to G1 (RR 2.38, 95% CI 0.78-7.24, p=0.126) (Table 3.4.2) (Figure 3.4.1 (b)).

Table 3.4.2: Incidence of allergic reactions per age group

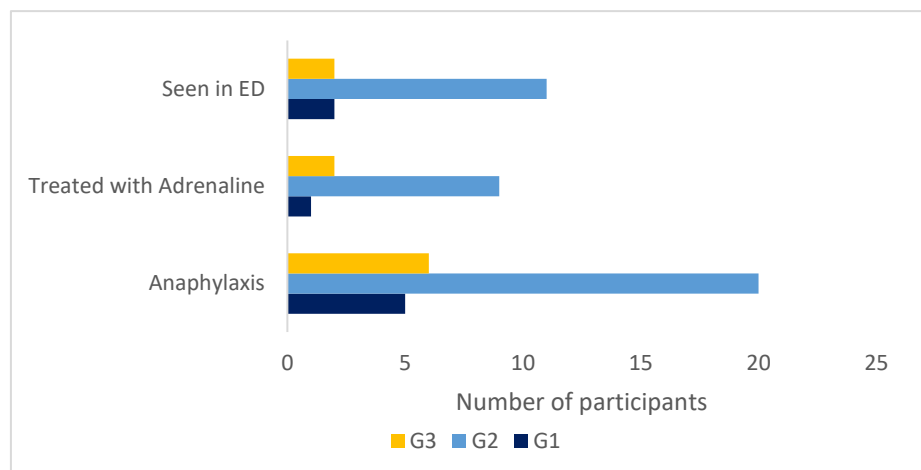
| Exposure | Incidence rate | (95% CI) |
|--|-----------------------|-----------------|
| All AARs | | |
| All | 0.44 | 0.38-0.50 |
| G1 (2-4 yrs) | 0.54 | 0.42-0.68 |
| G2 (5-12 yrs) | 0.39 | 0.32-0.47 |
| G3 (13-16 yrs) | 0.34 | 0.22-0.50 |
| AARs due to ingestion | | |
| All | 0.37 | 0.32-0.43 |
| Group 1 (2-4 yrs) | 0.42 | 0.31-0.54 |
| Group 2 (5-12 yrs) | 0.30 | 0.24-0.36 |
| Group 3 (13-16 yrs) | 0.29 | 0.18-0.43 |
| AAR defined as anaphylaxis | | |
| All | 0.062 | 0.042- 0.088 |
| Group 1 (2-4 yrs) | 0.038 | 0.012-0.089 |
| Group 2 (5-12 yrs) | 0.054 | 0.03-0.08 |
| Group 3 (13-16 yrs) | 0.079 | 0.028-0.17 |
| AARs treated in ED | | |
| All | 0.046 | 0.029-0.069 |
| Group 1 (2-4 yrs) | 0.015 | 0.0018-0.0055 |
| Group 2 (5-12 yrs) | 0.035 | 0.017-0.063 |
| Group 3 (13-16 yrs) | 0.026 | 0.003-0.095 |
| AARs treated with adrenaline. | | |
| All | 0.024 | 0.012-0.042 |
| Group 1 (2-4 yrs) | 0.014 | 0.0003-0.07 |
| Group 2 (5-12 yrs) | 0.029 | 0.013-0.055 |
| Group 3 (13-16 yrs) | 0.0262 | 0.003-0.095 |
| Abbreviations: AAR: accidental allergic reactions; CI: confidence interval; ; ED: emergency department; G1: group 1 (2-4yrs); G2: group2 (5-12yrs); G3: group 3 (13-16yrs) | | |

Figure 3.4.1 (a) % of children in each age group with reaction and (b) % of participants treated with adrenaline or attended the emergency department.

(a)



(b)



Legend figure 3.4.1

Figure (a) illustrates the % of participants in age group who had either any reaction (both anaphylaxis and non-anaphylaxis), anaphylaxis, or a non-anaphylaxis reaction

(b) Illustrates the % of participants who had a non-anaphylaxis or anaphylaxis reaction and their age group.

Abbreviations: G1: group 1 (2-4 yrs), G2: group 2 (5-12 yrs), G3: group 3 (13-16 yrs); ED: emergency department

Symptoms

Three quarters of participants had cutaneous symptoms, and a quarter had gastrointestinal symptoms. Thirty cases of anaphylaxis had documented symptoms consistent with both urticaria and/or angioedema as well as respiratory compromise (lower respiratory) as per NIAID criteria. Only 2 cases of anaphylaxis had symptoms indicative of cardiovascular compromise (collapse), one without respiratory compromise (Figure 3.4.2). There were 2 biphasic reactions.

Figure 3.4.2 Clinical features of the 220 allergic reactions

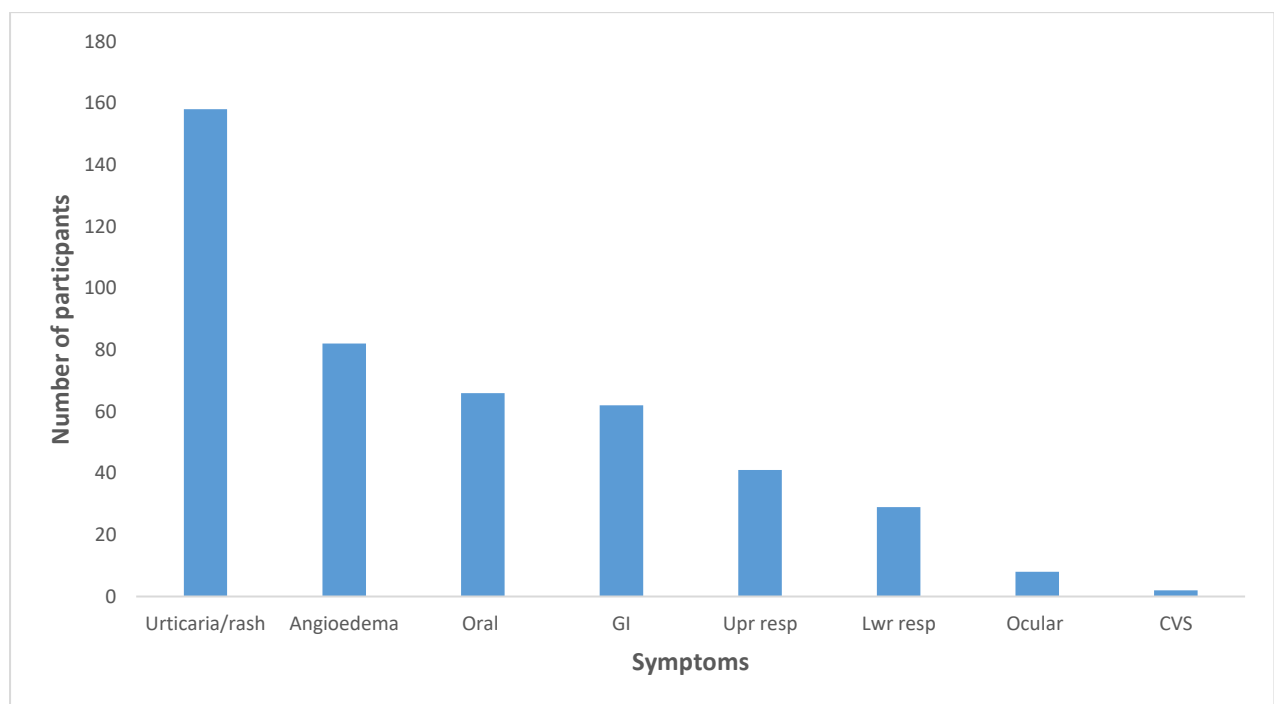


Figure 3.4.2 legend: This show the symptoms reported by participants in the 220 accidental allergic reactions
Abbreviations: GI: gastrointestinal; Upr resp: upper respiratory; Lwr resp: lower respiratory; CVS: cardiovascular

Management of the accidental allergic reactions

Most AARs were treated at home with 23 (10.5%) attending the hospital emergency department (ED). There were no intensive care admissions or hospitalisations (Figure 3.4.3). 91% of participants received medication to treat the reaction (table 3.4.3); 12 (39%) of the anaphylaxis cases and 1 non-anaphylaxis case received adrenaline (9 by parent, 4 by healthcare professional).

Eleven cases of anaphylaxis (35%) were treated exclusively at home (did not seek medical attention); 3 of these received intramuscular (IM) adrenaline by their parent; 7 children attended ED with symptoms of anaphylaxis and did not receive adrenaline (Table 3.4.3). As these children attended EDs across the country, it was not possible to review the notes the diagnosis made by the treating physician.

Figure 3.4.3: Management of accidental allergic reactions

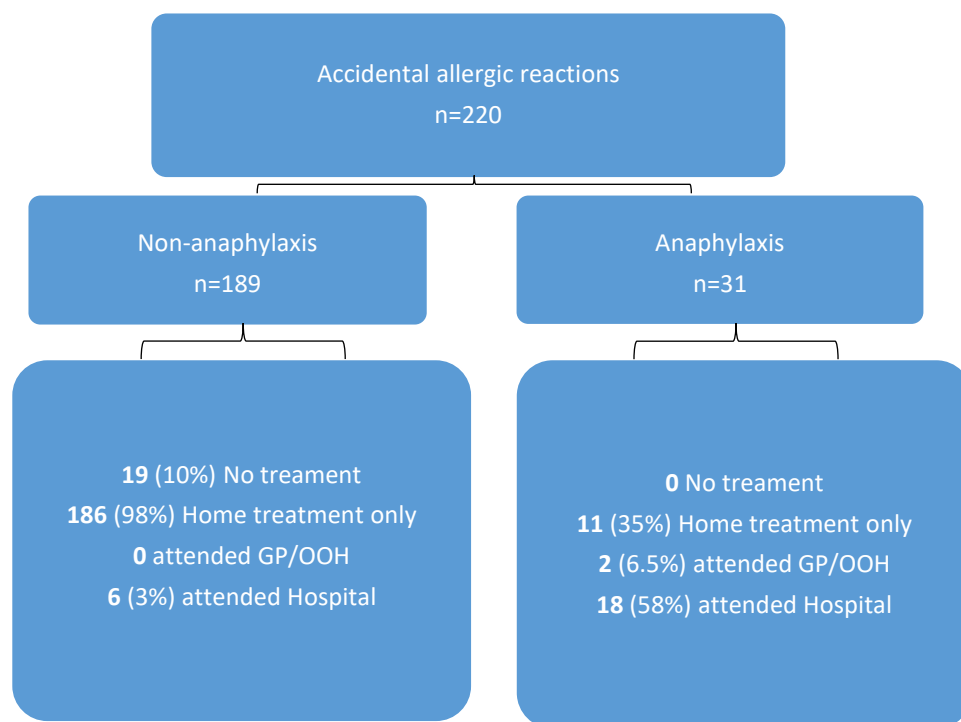


Figure 3.6: Legend: This shows the management of allergic reactions divided by non anaphylaxis versus anaphylaxis
Abbreviations: OOH: out of hours primary care

Table 3.4.3: Treatment of reactions

| | Overall N=220 | Non- anaphylaxis N=189 (86%) | Anaphylaxis N=31 (14%) |
|----------------------|--------------------------|---|-----------------------------------|
| No treatment | 19 | 19 | 0 |
| Antihistamine | 200 | 171 | 29 |
| Bronchodilator (inh) | 7 | 5 | 2 |
| Steroid (po) | 7 | 2 | 5 |
| Adrenaline IM | 13 | 1 * | 12** |

* n=1 administered by parent
 ** n=8 administered by parent, n=4 administered by healthcare professional
 Abbreviations: IM: intramuscular; inh: inhaler; po: oral

Route of allergen exposure

Overall, 187 (85%) reactions were due to allergen ingestion with the remaining 33 due to skin contact with the allergen. One third (n=12) of these reactions were due to skin contact with egg. There were no AARs due to inhalation.

Type of allergen involved in the accidental allergic reactions

The annualised incidence of nut reactions was 0.092 (95% CI 0.06-0.12); most nut reactions were due to peanut (41%) (Figure 3.4.5 (c)).

The allergen with the highest annual rate of AARs was cow's milk 0.32 (95% CI 0.20-0.46) (Table 3.4.4). Children in G1 were 4 times more likely to react to milk compared to those in G2 (RR 3.9, 95% CI 2.2-6.8, $p < 0.0001$). Children with cow's milk allergy (CMA) were significantly more likely to react as compared to children allergic to peanut (RR 5.24, 95% CI 3.05-9.01, $p < 0.0001$). The risk of anaphylaxis was higher for cow's milk as compared to peanut (RR 2.1, 95% CI 0.45-9.73, $p = 0.948$).

The most commonly identified trigger of AARs was hen's egg ($n=41, 18.6\%$) (Figure 3.4.5(a)). Participants reacted to egg in the following forms: baked $n=8$, lightly cooked $n=14$, almost raw $n=19$. The incidence for reaction to hen's egg was similar across all age groups: G1= 0.3, G2=0.2, G3 =0.12. Egg allergic children were also significantly more likely to react compared to peanut allergic children (RR 3.5, 95% CI 2.12-5.9, $p < 0.0001$). In contrast, the risk of anaphylaxis with egg was lower when compared to nut (RR 0.83, 95% CI 0.24- 2.90, $p = 0.78$) (Figure 3.4.4).

The highest percentage of anaphylaxis reactions per food allergen was to fish with 30% of reactions meeting the diagnostic criteria. Only 1 reaction to sesame seed was recorded from a total of 54 allergic children. It was categorised as non-anaphylaxis.

Overall, there were 5 reactions to fruit; 2 were reactions to peach, in children who were walnut sensitised. 3 met the criteria for pollen food syndrome (PFS); one AAR to apple (hives, mouth tingling), one reaction to melon (hives) and one reaction to kiwi (perioral hives, oral tingling). The remaining AARs were due to the following allergens: pea ($n=2$), soya ($n=2$), pumpkin seed ($n=1$), poppy seed ($n=1$), mustard seed ($n=1$) (Figure 3.4.5 (b)). (Of note, all of these participants were also allergic to at least one of the more common allergens: cow's milk, egg, peanut, tree nuts).

In 77 (37%) reactions, the allergen was unidentifiable.

There were 7 new (additional) allergic diagnosis made during the study, all subsequent to unexpected reactions. 2 were to fish, 2 were to cashew, in peanut allergic children, 1 to pulses and 2 to seeds. They all occurred at home and were all mild in character

Table 3.4.4: Annualised reaction rate per food allergen.

| Allergen | Reaction | Annualised rate of reactions | 95% CI |
|--|-----------|------------------------------|------------|
| All allergens N (%) | 220 | 0.44 | 0.39 -0.48 |
| Cow's milk N (%) | 25 (11.3) | 0.32 | 0.20-0.46 |
| Hen's Egg N (%) | 41 (18.6) | 0.22 | 0.15-0.29 |
| Fish N (%) | 10 (4.5) | 0.2 | 0.09-0.36 |
| Unidentified allergen N (%) | 77 (35) | 0.15 * | 0.39-0.62 |
| Any nut N (%) (Peanut, treenut, unidentified nut) | 46 (20.9) | 0.092 | 0.06-0.12 |
| Peanut N (%) | 19 (8.6) | 0.06 | 0.03-0.09 |
| Treenut N (%) | 15 (6.8) | 0.058 | 0.03-0.09 |
| Unidentified nut N (%) | 12 (5.5) | 0.024 | 0.01-0.04 |

*Denominator is total number of children with AARs

Figure 3.4.4: Severity of reactions to each allergen

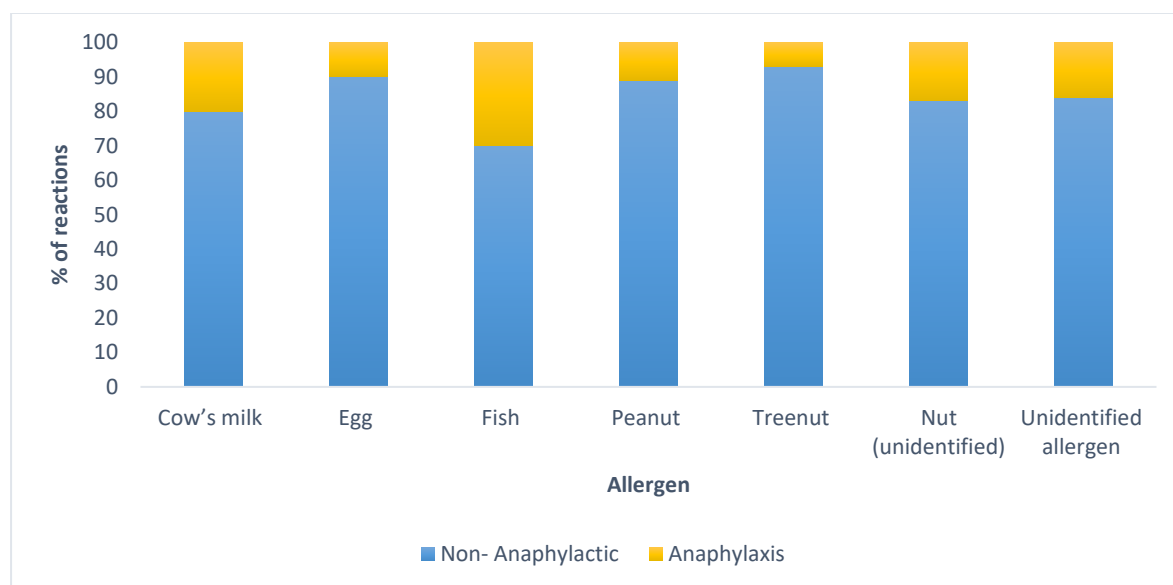


Figure 3.4.4 legend: This shows the proportion of reactions for each allergen that were anaphylaxis versus non-anaphylaxis

Accidental allergic reactions with an unidentified allergen

In 77 (35%) of the 220 AARs, the culprit allergen was not easily identified. All of these children had multiple allergies, therefore it was difficult to isolate the particular allergen. On review of the involved foods, the majority were cakes and confectionary which could contain cow's milk, hen's egg or nuts or a combination of allergenic triggers. The pattern of foods involved is very similar to the AARs where the allergen is identified with baked goods, biscuits and confectionary involved in 38 participants. Overall, 10 (13%) of these AARs were classified as anaphylaxis.

Figure 3.4.5 (a) Common allergen causing reactions, (b) Less common allergens causing reactions, (c) Type of nut causing reaction.

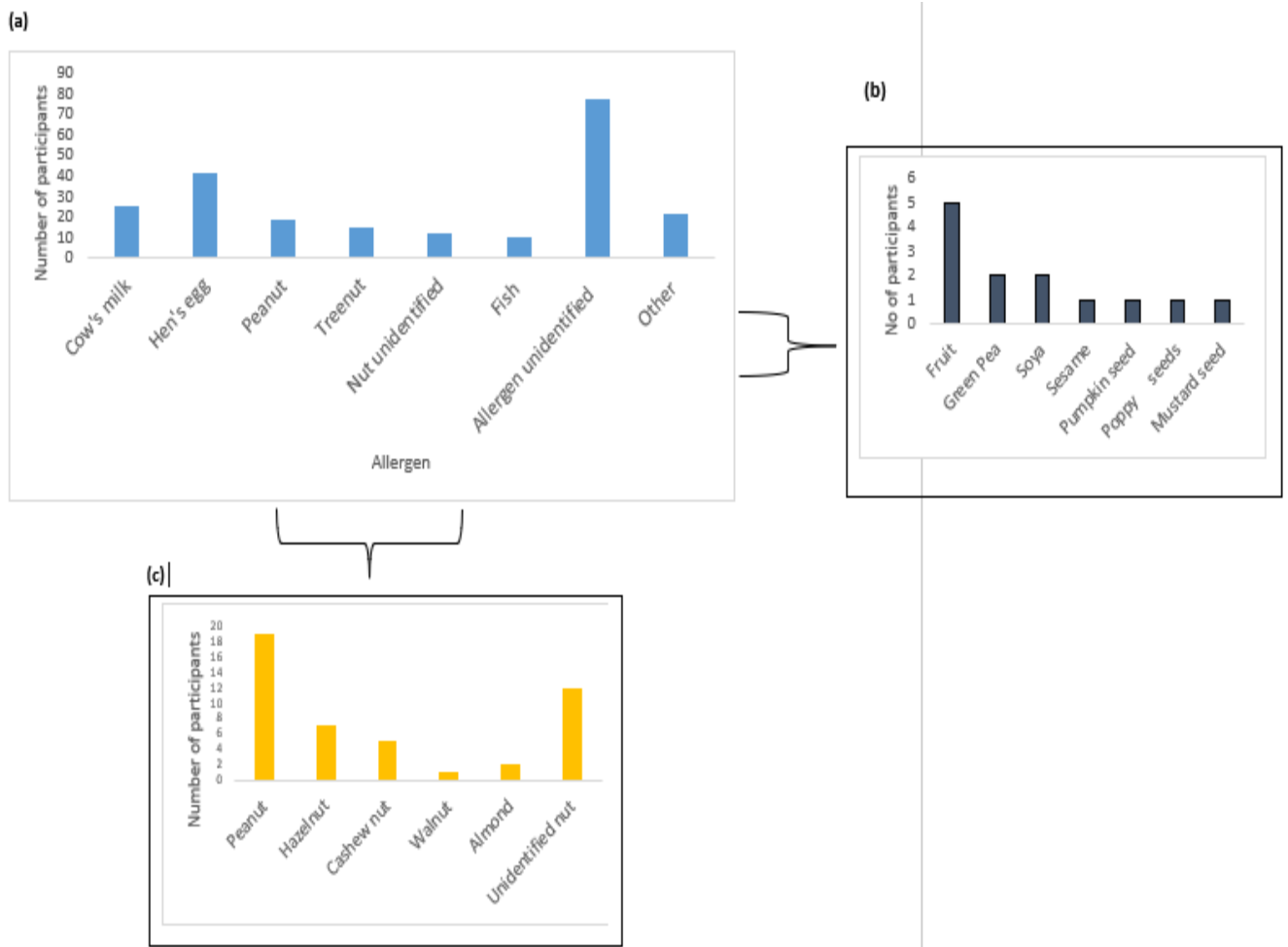


Figure 3.4.6 Allergens triggering anaphylaxis

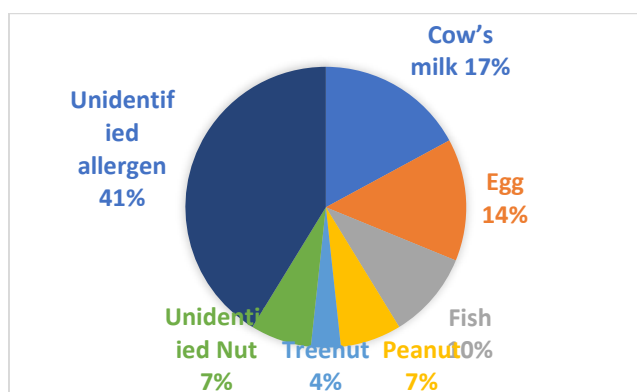


Figure 3.4.6 legend: shows the proportion of the anaphylaxis cases that are caused by each allergen

Table 3.4.5: Summary of reactions per allergen.

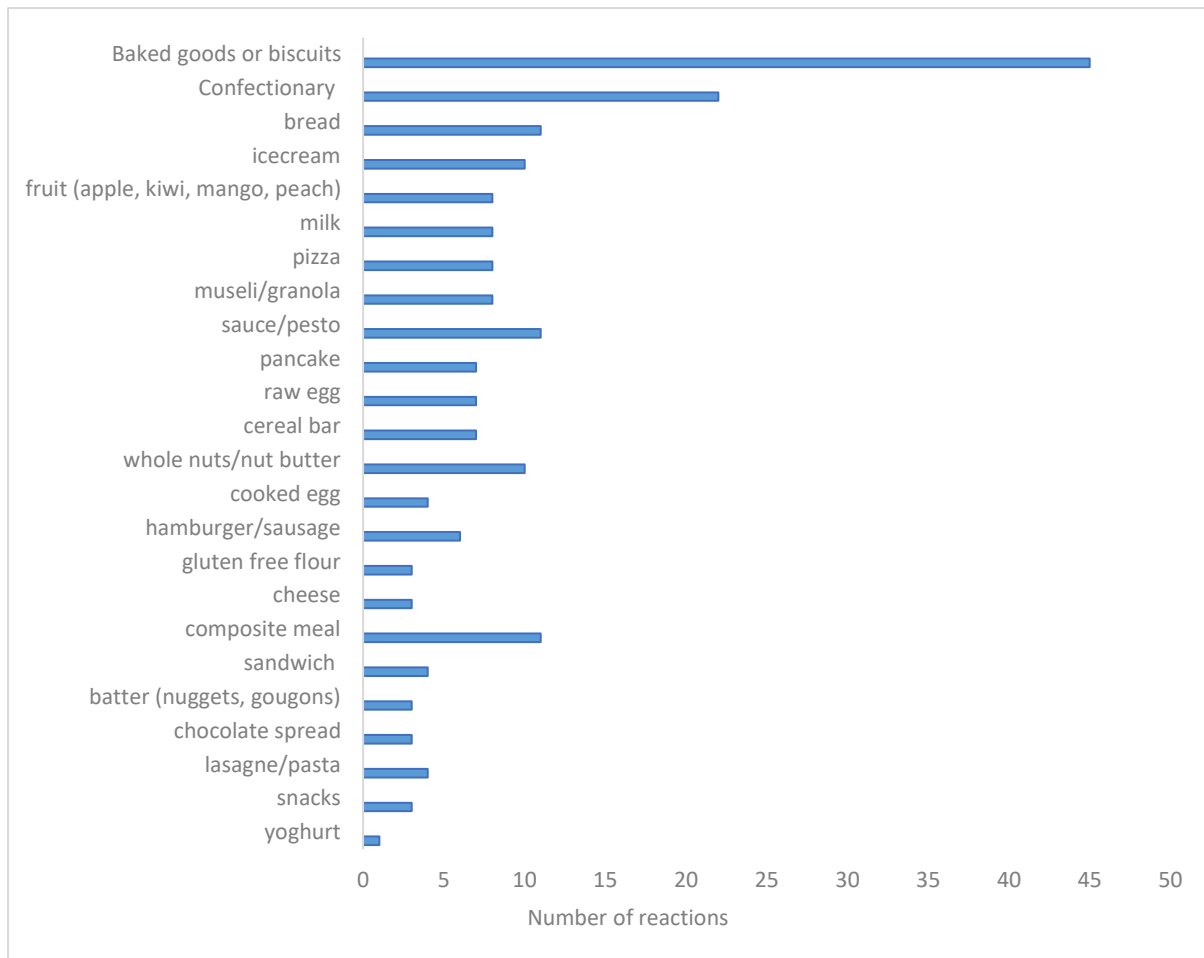
| | Overall | Non anaphylaxis N=189 (86) | Anaphylaxis N=31 (14) |
|---|---------|-------------------------------|--------------------------|
| All allergens n(%) | 220 | 189 (86) | 31 (14) |
| Cow's milk n(%) | 25 | 20 (80) | 5 (20) |
| Egg n(%) | 41 | 36 (88) | 4 (10) |
| Peanut n(%) | 19 | 17(89) | 2 (11) |
| Treenut n(%) | 15 | 14 (93) | 1 (7) |
| Nut (unidentified) n(%) | 12 | 10 (83) | 2 (17) |
| All nuts n(%) (PN, TN, unidentified nut) | 43 | 38 (88) | 5 (11) |
| Fish n(%) | 10 | 7 (70) | 3 (30) |
| Unidentified allergen n(%) | 77 | 65 (84) | 12 (16) |

Abbreviations: PN: peanut; TN: Treenut.

Food products causing reactions

Where the allergen could be identified (in 143 reactions), baked products (cakes, pastries, donuts, scones) (n=33, 23%), biscuits (n=12, 8.4%), confectionary (chocolate sweets, marshmallow) (n= 22, 15%) were the main implicated foods. Sauce or pesto (n=11, 7.9%), bread (n=11, 7.9%), Ice-cream (n=10, 7%), and pizza (n=8, 5.6%) caused a number of reactions (Figure 3.4.7).

Figure 3.4.7 Food product reported to cause reaction



Location of accidental allergic reactions

The most common location for reactions was at home; half of AARs (N=116, 53%) occurred there; 39 (18%) AARs occurred in food establishments (FE) (restaurants n=13, hotels n=9, fast food/takeaways n=10, cafés n=7). The next most common locations outside of the home, were school (n=18, 8.2%) and friend’s houses (n=11, 5%). The remaining AARs occurred in preschool childcare services (CCS) (n=6, 2.7%), relative’s houses (n=8, 3.6%), in/outside shops (n=3, 1.4%), airplane (n=3, 1.4%), airport (n=2, 0.9%) and finally n=1 in a playground. Of note, chapter 4 will discuss the school and preschool CCS AARs in detail.

The location of AARs in each age group was compared (Table 3.4.6). Participants in G2 were almost twice as likely to react in FE compared to G1 or G3 (RR1.79, 95% CI 0.92-3.45, p=0.08). G1 were 3 times more likely to react in a relative’s house as compared to the older children in G2 and G3. (RR3.49, 95% CI 0.85-14.22, p=0.08). G3 were significantly more likely to have a reaction in a

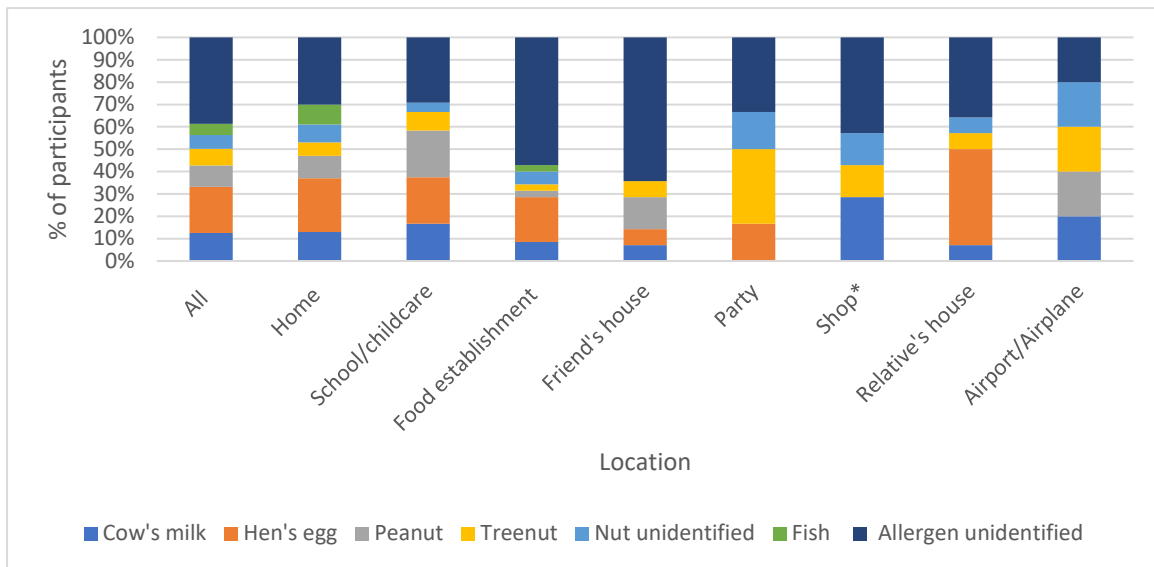
shop/or eating shop bought food compared to G1 and G2 (RR 4.45, 95% CI 1.13- 17.55, p = 0.032). They were also more likely to react in a friend's house (RR 2.47, 95% CI 0.71- 8.55, p= P = 0.152) or at a party (RR 2.96, 95% CI 0.60-14.53, p= P = 0.179).

Table 3.4.6: Location of reactions per age groups

| | Overall N=220 | Group 1 N=71 (%) | Group 2 N=123 (%) | Group 3 N=26 (%) |
|---|--------------------------|-----------------------------|------------------------------|-----------------------------|
| Home n(%) | 116 (53) | 37 (52) | 66 (54) | 13(50) |
| Food establishments (Restaurants, café, fast-food, hotel) | 36 (16) | 10 (14) | 26 (21) | 3 (12) |
| School | 18 (8.2) | 0 | 16 (13) | 2 (7.7) |
| Friend's houses | 11 (5) | 5 (7) | 4 (3.2) | 3 (12) |
| Shop bought food | 8 (3.6) | 3 (4.2) | 2 (1.6) | 3 (10) |
| Relative's house | 8 (3.6) | 5 (7) | 3 (2.4) | 0 |
| Party | 7 (3.2) | 2 (2.8) | 3 (2.4) | 2 (10) |
| Preschool childcare services | 6 (2.7) | 6 (11.3) | 0 | 0 |
| Airplane | 3 (1.4) | 1 | 2 (1.6) | 0 |
| Airport | 2 (0.9) | 1 | 1 (0.8) | 0 |
| Playground | 1 | 1 | 0 | 0 |
| Abbreviations: G1: group1 (2-4yr); G2: group 2 (5-12yr); G3: group 3 (13-16yr). | | | | |

The breakdown of the locations of the reactions due to an unidentified allergen were different to the overall cohort. More of these AARs occurred in FE (40%) with only 35% occurring in the home. Most cases of anaphylaxis occurred at home (48%) with school /childcare and FE the next most common locations (16% each) (Figure 3.4.10).

Figure 3.4.8: Allergen causing reaction by location



Legend: Figure 3.4.8 illustrates the proportion of participants reacting at each location for each allergen.

All= Allergens causing all reactions irrespective of location.

*Shop: participants had bought food from a shop and then ate it on leaving the shop in transit- in car, walking, sitting outside.

Figure 3.4.9: Location of reaction per reaction grade

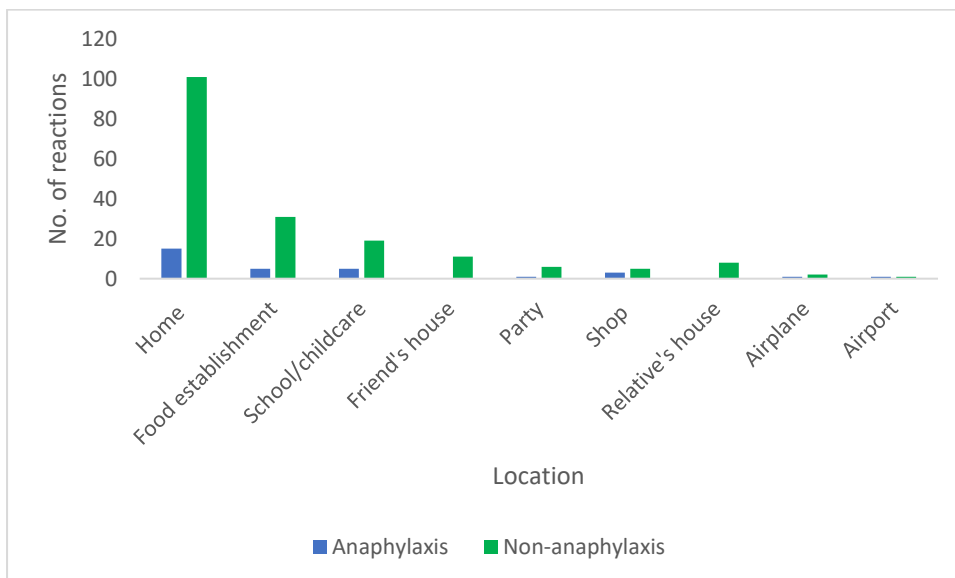


Figure 3.4.9 legend: this shows the proportion of reactions that occur in each location divided by severity.

Figure 3.4.10: Location of anaphylaxis

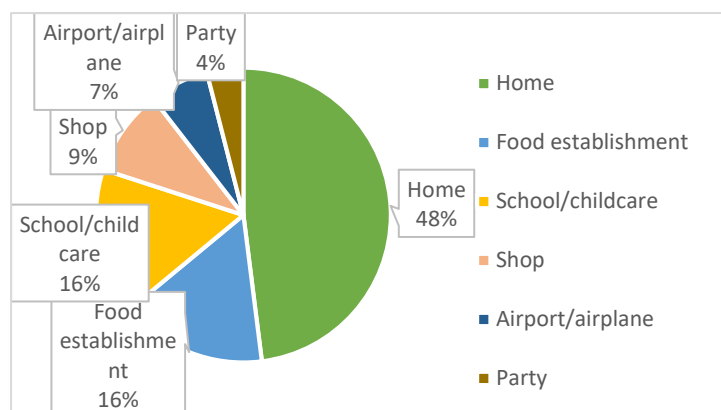


Figure 3.4.10 legend : shows the locations of the 31 cases of anaphylaxis. Almost half occurred at home

AARs in food establishments

Food establishments were the second most common site of reaction with 36 (16%) AARs occurred in some type of eatery (restaurants n=13, hotels n=9, fast food/takeaways n=8, cafés n=6). A quarter of reactions in eateries were due to hen's egg. In over a third, the allergen was not easily identified (Figure 3.4.11). Overall, the ingredients were asked for in 63% (n=23) of reactions; however wrong/incomplete information was given (n=10). In the remaining 13, the food ingested was potentially contaminated with allergen (n=13). In 37%, the ingredients were not looked for. 61% of the reactions arising in FE, occurred while on holidays. Looking specifically at the reactions in restaurants, 12/13 occurred while on holidays. 13.8% of the AARs occurring in FE were anaphylaxis.

Figure 3.4.11: Allergens in food establishments

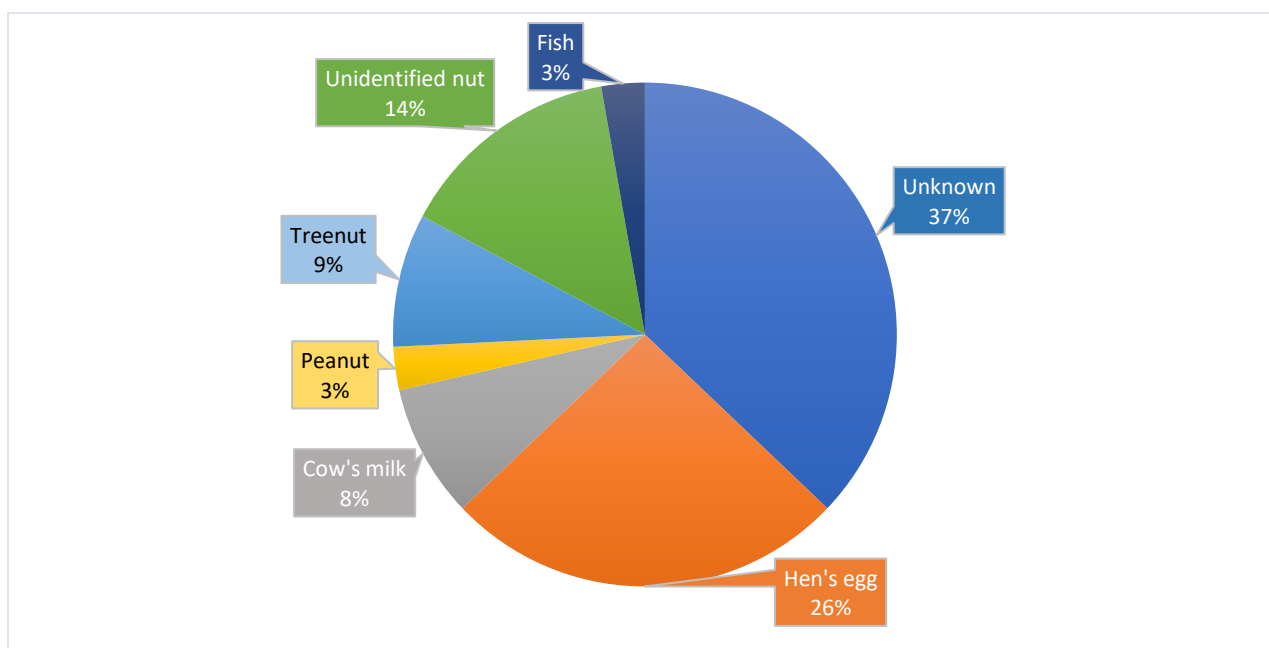


Figure 3.4.11 legend shows the allergen causing the 36 reactions in food establishments. Over a third were unknown

Table 3.4.7: Examples of errors made in food establishments

| Consumption of food containing allergen | Contamination of food with allergen |
|---|---|
| Nuts within sprinkles on top of ice cream | Ice cream scoop previously used for nut ice cream in a café |
| Pesto (containing cashew nut) within sandwich | Ate muesli at hotel buffet (contaminated with nuts) |
| Salad dressing contained nuts | Pizza contaminated with allergen (nut) |
| Stew sauce contained cow's milk | Burger contaminated with allergen (? Egg or sesame) |
| Soya sauce within meal in Asian restaurant | |
| Brownie contained nuts | |
| Fresh bread (contained cow's milk) from café | |
| Pizza contained egg (given wrong information from server) | |
| Ate cookie from fast food restaurant (contained egg) | |
| Ate muffin containing peanut in cafe | |

Identified provider of the allergen containing food

In 92 (47%) of AARs, the parent of the child accidentally administered the allergen containing food. Other people who were involved in giving the allergen to the child: child themselves (n=39), friend (n=12), sibling (n=5), teacher/childcare worker (n=7), relative (n=5), friend's parent (n=9), server in FE (n=36), other (n=15).

Factors contributing to the accidental allergic reactions

An attempt was made to identify a cause for the reactions. Human error was considered a contributor in half of reactions. Other factors included: didn't check ingredients (n=51), did check ingredients/ possible cross contact with allergen (n=40), label reading errors (n=2) (Table 3.4.8). In 8 cases, the AAR was due to a new food allergen. However, all 8 of these participants had other known allergens and already carried adrenaline autoinjectors. There was a higher number of children who reacted in G1 whose parents reported they did not check the ingredients compared to parents in G2 (p=0.08). More unusual allergens were new exposures e.g. pumpkin seed, poppy seed mustard seed.

Table 3.4.8: Contributing factors in the 220 reactions

| | N | Human error N=110 (50%) | Did not check ingredients N=51 (23%) | Did check ingredients N=40 (18%) | New allergen N=8 (4%) |
|--|----------|------------------------------------|---|---|----------------------------------|
| Overall N (%) | 220 | 110 (50) | 51 (23) | 40 (18) | 8 |
| Cow's milk N (%) | 25 | 16 (64) | 6 (24) | 3 (12) | 0 |
| Hen's Egg N (%) | 41 | 25 (61) | 11 (27) | 3 (7) | 0 |
| Peanut N (%) | 19 | 7 (44) | 7 (44) | 2 (13) | 0 |
| Treenut N (%) | 15 | 5 (33) | 6 (40) | 1 (6.6) | 2 |
| Unidentified nut | 12 | 6 | 4 | 2 | 0 |
| All nuts N (%) (PN, TN, Unidentified nut) | 46 | 18 (42) | 17 (40) | 7 (16.3) | 4 (9.3) |
| Fish N (%) | 10 | 5 (50) | 0 | 4 (50) | 2 (20) |
| Unknown N (%) | 77 | 34 (44) | 14 (18) | 20 (26) | 1 |

Accidental allergic reactions during special occasions or cultural holidays

Overall, 18 (8.2%) of reactions occurred at a special occasion or during a cultural holiday; 6 occurred at a birthday party, 2 occurred at a First Holy Communion celebration, 3 at a wedding, 2 on Pancake Tuesday, 2 at Halloween, 1 at Christmas. 5 of 18 were also reactions that occurred within an eatery. There were no AARs documented at Easter or during Eid al-Fitr. A quarter of these occurred in food establishments (wedding n=3, First Holy Communion n=2).

Accidental allergic reactions in ethnic minorities.

There were 18 reactions among participants of African or Asian ethnicity. The annualised AAR rate in this group was 0.40 (95% CI 0.242- 0.646) which was not significantly different from the rate in Caucasian Irish (p= .485). There was a slightly higher number of severe reactions in the ethnic minority group compared to Caucasian (RR 1.20, 95%CI 0.40-3.57, p=0.332).

Accidental allergic reactions occurring while on vacation

Overall, 403 (80.9%) participants went on vacation during the study period with 244 (60.5%) going abroad (235 on airplane, 9 on ferry); 307 (76%) stayed in hotels; 115 (47%) ate food bought in the airport before flying, 90 (36%) only ate food from home in the airport with the remaining not eating at all in the airport.

Overall, 33 (15%) children had AARs on vacation; this gives an annualised AAR rate while on holiday as 8.2% (95% CI 5.7 to 11.3); 18 (66%) occurred in locations where English was not the first language; 15 of these 18 occurred while on holiday in Ireland. Participants were more likely to react on holiday abroad compared to holiday in Ireland ($p=0.219$).

These AARs were graded as non-anaphylaxis ($n=24$) or anaphylaxis ($n=9$). There was a significantly higher number of severe reactions while on vacation compared to those that did not occur on holiday (RR 2.3, 95% CI 1.17-4.58, $p=0.0156$). Adrenaline was administered in 2/9 of the anaphylaxis cases. In nearly half ($n=14$, 43%), the implicated allergen was unidentified. The identified allergens were: nut $n=6$; cow's milk $n=5$, hen's egg $n=3$, fish $n=2$. The main types of food involved were: ice cream ($n=3$), cakes ($n=6$), pizza ($n=5$), chocolate ($n=2$), fish ($n=2$).

Reactions occurred in restaurants ($n=12$, 36.3%), hotels ($n=8$, 24%), shop/ café ($n=7$, 21%), airplane ($n=3$, 11%) and airport ($n=2$, 6%). Of note no reactions occurred in self-catering accommodation. But 3 of the 12 reactions occurring in restaurants were in participants staying in self-catering. Participants staying in hotels were more likely to have a reaction compared to those in self-catering accommodation ($p=0.110$). In almost half of reactions ($n=15$, 45.5%), participants had asked about or checked ingredients. Of the 235 who travelled by airplane, 3 (12.7%) had AARs (Table 3.4.9).

Table 3.4.9: Reactions occurring on airplanes and in airports .

| | Case 1 | Case 2 | Case 3 | Case 3 | Case 5 |
|---|---|--|-------------------------------|--------------------------------------|--|
| Location | Airport | Airport | Airplane | Airplane | Airplane |
| Age (yrs) | 3 | 5 | 8 | 5 | 2 |
| Circumstances | Sandwich bought in airport by parent; ate in airport. | Pizza bought in airport and eaten in airport | Ate meal provided on airplane | Sandwich made and brought from home | Packaged GF sandwich brought from home |
| Checked ingredients | No | Yes | Yes | Yes | No |
| Allergen involved | peanut (within pesto) | Unknown* | Unidentified nut | Peanut | Cow's milk (in gluten free flour) |
| Length of flight (hrs) | 4 | 1 | 4.5 | 1 | 2 |
| Anaphylaxis | No | Yes | No | Yes | No |
| Treatment | AH | AH (child refused AAI) | AH | AAI on airplane (given by parent) | AH |
| Informed aircraft staff during reaction | No | No | No | No | No |
| | * child was allergic to peanut and hazelnut Abbreviations: AAI: adrenaline autoinjector, AH: Antihistamine, GF: gluten free. | | | | |

SECTION 3.5: DISCUSSION

This study shows that accidental allergic reactions (AARs) are not an infrequent occurrence among Irish children with an overall annual incidence of 0.44. This figure is comparable to the incidence reported from the UK in a recent, multisite, survey-based analysis of accidental reactions (14). This multisite study also highlighted a variability in AAR incidence across regions with an incidence of only 0.3 recorded in the US. The similarity between the UK incidence rate and our findings may reflect comparable eating habits and less awareness in the community (food establishments) regarding FA (14).

In ReAACT, 31% of participants had at least one reaction/year. A recent study published this year of 2679 participants (2510 <18yr) in USA, recruited from a patient registry found that over 50% of participants reported at least one AAR/year (120). Although this study was retrospective and included participants with self-reported FA, it includes all reactions inclusive of those that resolved at home which is comparable to our work. The number and type of allergens studied as well as the method of FA diagnosis can affect the incidence of AARs reported. Studies that look specifically at nut reactions will report a lower AAR rate. To emphasise this, we calculated an annual incidence for each different allergen (Table 3.4.4). Annual incidence rates of peanut/nut AARs among physician diagnosed participants are reported as: UK (3%) (13), Canada: 14.3% (128), 11.9%(146), USA: 4.7% (15). In ReAACT, it was 9.2%, comparable with the Canadian figures but higher than figures above from the UK and USA. Comparisons are difficult between studies due to methodological differences as outlined in the literature review. ReAACT data also includes all food reactions, including contact reactions (which accounted for 15% of the total). We did however calculate the incidence of reactions due to ingestion and found it not to be substantially lower (0.37, 95% CI 0.32-0.43) than the overall rate of reaction. The participants in our study were recruited from tertiary allergy clinics; over two thirds had ≥ 2 food allergies and a quarter had a history of anaphylaxis. Multiple food allergies (12, 14, 131) and a history of anaphylaxis (16) have previously been reported as risk factors for AARs. In addition, we used a strict definition of FA. This was to ensure that all participants were food allergic and therefore at risk of AARs. This contrasts with a number of other studies where self-reported FA was used to define FA (86, 139). Gupta et al recently found that half of respondents in their survey in USA were self-reported and had never been confirmed by a physician (160). Having participants in a study that are not truly allergic will lower the incidence as the denominator is diluted by those not at risk of reactions. Regular follow up with these participants (every 3 months), ensured that even small mild reactions were recorded, many of which may have been forgotten by the next clinic appointment. In addition, the fact that these children were in a study monitoring AARs meant that many parents

were keeping a written record of reactions to aid with recall. This contrasts with retrospective studies that report “every” having a reaction”(133, 134, 152); there may be significant lag time (sometimes years) between the reaction and reporting.

The impact of the COVID-19 imposed lockdown, finalised on March 24th, 2020, on the annual incidence is difficult to define. The overall annual incidence calculated for those followed only during “normal circumstances” (outside of pandemic), did not differ from the incidence rate for all participants. A reduction in reported reactions was noted when comparing the first, second and third quarters with the fourth quarter of the study. However, the difference was only found to be statistically significant when compared with the first quarter. It is reasonable to propose that the risk of location-specific reactions, such as those in eateries and schools would have reduced. Nevertheless, many cafes and restaurants were still open for takeaway and so the potential for eatery related reactions remained. School and creches were closed for an extended period. However, under normal circumstances, 2 weeks of school holidays would have been scheduled during April also. COVID will have impacted little on travel/vacation related as most of the families involved would not have travelled until the summer holidays. International data assessing this issue is limited and conflicting. A Canadian study of allergic presentations during COVID found that the number of food related reactions presenting to an emergency department was no different to the same time period a year earlier (161) (3). However, an Israeli study reviewing reactions over a short time (median 6 weeks) has suggested there was considerably less reactions during lockdown (162).

We report a significantly higher incidence of reactions in younger children (0.54) as compared to children 5-16 yrs (RR 1.4, 95% CI 1.14-1.71, $p=0.001$). Fleischer et al report an even higher annual incidence (0.81, 95% CI 0.76-0.85) in their cohort of younger children (3-15months). More of this age group were milk and egg allergic which were the cause of over half of the total reactions. Although the incidence of egg reactions was similar across the 3 age groups, children in G1 were 4 times more likely to react to milk compared to those in G2 (RR 3.9, 95% CI 2.2-6.8, $p<0.0001$). This is further backed up by the fact that studies only reporting on nut AARs, have a lower AAR rate in younger children (48). In addition, younger children are not developmentally mature to regulate their behaviour, communicate their allergy and avoid allergenic foods themselves putting them more at risk from accidental exposure. We report the annualised incidence of reactions in the adolescent group as lower than the children in G1 and G2 ($P = 0.155$). This compares with a recent multisite retrospective study of self-selected participants, which reported a significantly lower annual rate of reactions in adolescents versus children (0.21 vs 0.41, $P<0.0001$) (14). However, as adolescents spend more time away from their parents, they might not inform them

of all of their reactions. One study reported that adolescents do not inform their parents of 12% of reactions (110). However our findings do contrast with other studies which report higher numbers of AARs among adolescents (16, 163).

In this study, anaphylaxis was defined using the NIAID criteria (123). The severity of each reaction was determined retrospectively using information provided by parents. It is possible that the number of cases of anaphylaxis may have been exaggerated. However, collecting the information through a phone-based discussion through which clarification and detailed questioning was possible, is likely to have improved accuracy. Using the NIAID criteria has previously been shown to reduce retrospective overestimation of anaphylaxis (116). The overall annualised incidence of anaphylaxis related to accidental ingestion was 0.062. The rate was higher in adolescents at 0.079. This contrasts with the recent survey-based publication by Venter et al in which significantly less adolescents reported severe reactions compared with younger children. However, they also reported that significantly more adolescents reported receiving adrenaline suggesting that the families were under reporting symptoms (14). The findings of our study are, however, consistent with other publications reporting adolescents having more severe reactions and a higher number of fatalities (154, 164-166).

This study has provided a detailed understanding of location and risk of AARs specific to our population. Although reactions were identified in association with all cultural holidays and celebrations that were inquired about, only 2 reactions were reported during Halloween activities, which almost all of our age-appropriate study candidates took part in. No reactions were reported at Easter. This contrasted with a 10-year retrospective report from the Canadian anaphylaxis registry which reported a 70% increase in anaphylaxis at Halloween and Easter (45). Their study included first reactions which are likely to occur due to opportunistic exposure to peanuts and tree nuts.

The data presented here, establishes that travelling on vacation is associated with a significantly increased risk of severe allergic reactions than staying at home. AARs occurring while on holiday or vacation is an area that has not previously been well researched, particularly in children. The majority of this study cohort travelled on holidays allowing for a closer examination of effect on accidental reactions. The data indicates that causation may be due to increased risk related to eating out while on holidays as almost all reported restaurant related reactions occurred while on holidays. It is reasonable to presume that language barriers may have contributed to this observed increase in restaurant related reactions. However, despite a higher number of reactions being recorded on holidays abroad compared with holidays in Ireland, significance was not

demonstrated. It is likely that multiple factors contributed. It will be important going forward to encourage families of allergic children to avail fully of the safer option of self-catering where no reactions were demonstrated.

Accidental reactions aboard planes have been studied in more detail and more recently the risk of airport food has been highlighted by a fatal anaphylaxis to sesame seed of a British school girl. Recommendations regarding risk reducing measures have been published and have always been part of the education provided by our allergy department with particular focus being placed on the potential risk of food purchased in airports and onboard planes. The fact that 2 of the 5 airport/aeroplane reactions recorded in this study occurred after ingestion of food brought from home, demonstrates the challenges to prevention of travel related reactions. Barnett et al report that people use adapted versions of their own allergen avoidance strategies while on holidays in recognition of the enhanced risk of AARs while travelling (167). However, there appear to be so many so many factors including lack of concentration during preparation and cross contamination during eating, that have to be considered.

In chapter 2, it was highlighted that a greater number of enrolees reported routinely bring their own food to friends' houses and parties than to eating establishments. Fast food outlets were particularly notable in that they were attended by all age groups, the majority of whom reported eating food prepared on site. We proposed that this differential behaviour may be due to a belief that more control can be applied over food preparation in a restaurant than a domestic environment such as a friend's house or a party. In this chapter, friend's homes were identified as a source of accidental ingestion, with adolescents being significantly more likely to be involved than younger children. The second most common locale for AARs was eating establishments. However, as highlighted above, most restaurant related reactions occurred while on holidays. Nevertheless, 8 mild reactions were recorded in fast food outlets. Shops, where in theory, where more control is exertable through label reading was the location for almost 10% of anaphylactic events.

In chapter 2, details were also captured, regarding sub-cohorts, particularly adolescents with a history of peanut anaphylaxis, not engaging in any eating practices outside of home. Additionally, almost a ¼ of the entire study group brought food prepared at home when going out to eat. In this chapter it is shown that the most common setting for accidental reactions is in fact the home. This is reported almost universally across the literature (13, 14, 16, 28, 88, 120, 138, 139, 144). Furthermore, it is also the primary setting for anaphylactic reactions (45%); a figure similar to previous reports of anaphylaxis: 46% (141) and 53% (127). This likely reflects the fact that children

consume most of their food at home and therefore the probability of a reaction occurring here is higher than in other places.

Collectively, this data teaches that imposed harsh restrictions on allergic children do not necessarily limit risk. Conversely it also teaches that perception of control and safety is misleading and that therefore a constant readiness to respond to allergic reactions is paramount.

Anaphylaxis was under-treated in this study. Only 39% (12/31) of cases of anaphylaxis were administered adrenaline. This low number mirrors the results of many other studies in this area with rates of between 11 and 71% reported. The wide range in numbers is influenced by way the data is collected and reported. Those studies which look at rate of adrenaline administration per food anaphylaxis case (not location dependant), report rates of between 30-43% (16, 120, 131, 132, 139, 168). Only one AAR was considered to be over-treated in this study; adrenaline was administered for a mild non-anaphylactic reaction. Higher levels of over-treatment with adrenaline have been reported; a Swedish report of paediatric presentations of food reactions to 3 EDs, found that 70 of 371 reactions reviewed were administered adrenaline (either at home, enroute or in hospital), however their symptoms did not meet the criteria for anaphylaxis (169). They do make the point that the adrenaline may have halted progression to anaphylaxis. The data shows that anaphylaxis is either not being recognised by the parents of this cohort or they are hesitating to use. Only 9/31 (29%) cases were administered adrenaline by the parent. This is not a unique finding. A Canadian review of nut anaphylaxis cases, found only 11% received adrenaline outside of hospital (18). The European registry of anaphylaxis, which includes Irish data, reported in 2016 that a third of anaphylaxis in children and adolescents were treated by laypersons (33). The results demonstrate that continued optimisation of education is required within the clinic setting. The model used at the time of enrolment was face to face training with an allergy doctor or nurse specialist. This technique has been shown to be superior to other models using simulation studies (170). However, these scenarios do not fully reflect a real-life environment where other factors may come into play. A community-based survey from 2009 identified uncertainty about the severity of the reaction and fear of side effects as reasons for not applying autoinjectors (171).

The identified allergen causing the highest proportion of anaphylaxis cases per allergen was fish (30%) with cow's milk a close second. However, numbers of cases with fish allergy were small and Cow's milk was the allergen with the highest annual rate of AARs for identified allergens (0.32) with fish at only 0.22. In ReAACT the risk of anaphylaxis was greater in those with milk allergy than those with egg or peanut allergy. The European Anaphylaxis Registry reported on reactions in children and adolescents in 2016 (Cow's milk and hen's egg were prevalent elicitors in the first 2

years, hazelnut and cashew in preschool-aged children, and peanut at all ages (172). The registry includes all cases of anaphylaxis and not just those in children already practicing avoidance. A Swedish review of all anaphylaxis cases (accidental and unexpected) presenting to Emergency Department (ED) department in children, found milk was the most frequent allergen (32%) with peanut second (21%) and unidentified allergen (16%)(173). In contrast, a Canadian review of 168 paediatric presentations to the ED of children with anaphylaxis reported that most reactions were to nut (142). Unidentified allergens contributed to 41% of anaphylactic reactions in ReAACT. International data on this issue is variable. In a study of ED presentations of anaphylaxis, it was reported that the trigger allergen was only known in one third of cases of anaphylaxis (174). However, another ED review of 168 anaphylaxis presentations found an allergen to be identified in 75% of cases (142). In a review of fatal anaphylaxis cases in the UK over 7 years, 38% of cases occurred to an unknown allergen (154).

Unidentified allergens were not just associated with severe reactions in our study. 35% of overall reactions were concluded to be without an identifiable trigger, despite reasonable efforts to identify one as detailed in the methods. This inability to isolate a particular allergen is infrequently reported in the literature, albeit referenced in 3 publications above. This may be due to how the data is reported. In studies where the participant self-reports the data, there may have not been an option to answer, “unknown allergen”. In this study, a discussion was had between participant and researcher, allowing for extra information to gathered, however this did not help to isolate the trigger in a third of cases. It is very likely that many of these reactions in this study were due to cross-contamination. This is supported by the fact that the commonest locations for these reactions to occur was in food establishments (FE) and friend’s houses where food is prepared by others. Indeed, we concluded that cross-contamination was the likely cause 13/36 (36%) AARs in FE, as correct ingredient information had been provided. A study of AARs in American restaurants found that 13% of reactions occurred even when ingredients were checked and waiting staff informed (88). The scale of this issue is unknown; there is a paucity of literature on the frequency of allergic reactions caused by cross contamination; Taylor et al highlight that the risk associated with cross-contamination is dependent on many things including the patient’s threshold dose. A Dutch study analysed food samples received from 51 adults after an allergic reaction; 37% of products analysed had 1 to 4 culprit allergens identified that were not supposed to be present according to the ingredient declaration (149). Bread, cookies, chocolate, and meat were implicated in 53% of foods with undeclared allergens. The first 3 were the foods implicated in over half the reactions in ReAACT too.

Some of these individuals may have been reacting to new allergens. Testing for this is difficult unless there is a high suspicion of one particular ingredient, as sIgE testing and /or skin prick testing to numerous ingredients without a preformed hypothesis leads to overinterpretation of sensitisation. This is further complicated by the fact that allergic individuals may also have reactions due to cross reactivity that can be difficult to recognise without detailed ingredient information. In particular, there is a high degree of protein sequence homology between the seed storage proteins in peanuts and treenut. The abundance of homologous allergenic proteins in plant material (edible foods and pollens/aeroallergens), their relative abundance in specific foods, their variation in heat stability as allergens, and degree of homology as well as other factors creates a range of clinical outcomes (36); Another point to raise is the concomitant exposure of food allergens with pollen and whether pollen acts as a co-factor. A Swedish review of anaphylaxis cases presenting to a paediatric ED, found that pollen-allergic children seemed to be admitted due to food-induced anaphylaxis more often during the deciduous tree pollen season compared with the rest of the year and they suggest that concomitant exposure to airborne allergens seems to increase the risk of anaphylaxis to foods (143).

An important finding in this study was that the parent administered the allergen accidentally in 92 (47%) reactions. The number was less for anaphylaxis (39%), but this was not statistically significant ($p=0.77$). This information has only been reported in 2 studies that the author could find, one was a study of infants (parents administered it in 48% of cases)(132) and the other was a UK study of nut reactions (parents 41%) (13). It is important for 2 reasons. Firstly, it is useful for us to be able to tell parents that if their child has a reaction, they are likely to be there. This is not to cause guilt but to empower parents that they will be present and able to keep their child safe by appropriately managing the reaction which they have been educated to do. Secondly, it underpins emphasises the unavoidable and accidental nature of reactions. Parents, who are most invested in their children's safety are implicated as a contributing factor in half of the reactions.

Other identified contributing factors included a failure to read ingredients. A quarter of participants acknowledged that ingredients were not checked prior to the child consuming the food. 2 admitted to an error in reading a food label, but as 20% reported that they had read the ingredients, this number may represent an underestimation. Fierstein et al found a similar number (21.5%) had checked ingredients and that allergen was not identifiable (120). A previous study has shown that 40% of food allergic participants, found labelling particularly precautionary allergen labelling (PAL) unclear (175). A UK study reported that 40% of reactions were caused by contact with nut traces, however there is no descriptions given how they quantified this and what the context of the ingestion was (176). Half of reaction in ReAACT were concluded to be due to

human error. Human error, as a common cause of reactions, is supported by what we see within the strict settings of RCTS trials. In Palisade, the pivotal oral peanut immunotherapy (IMT) study, all adverse events were studied; 19.6% of actively treated subjects and 33.1% of placebo treated subjects reported accidental exposures to any food allergen during the study (112). Further research into behaviour modification is required to reduce this risk. This study did not aim to investigate this issue. However, there is a key take away message for allergic families regarding human fallibility and how it justifies carrying autoinjectors at all times.

The study data indicates that protecting the host(allergic child) by controlling their environment is a flawed model. Thus focus needs to be turned on protection through manipulation of the hosts own defences. Promotion of tolerance to allergens through early introduction and desensitisation is now a key component of international allergy care. Part of this evolving strategy is the acceleration of natural tolerance to cow's milk and egg by introduction of baked forms of both to young infants. Recent unpublished data from this centre has demonstrated the effectiveness of the Milk Ladder in this regard. In ReAACT it was seen that reactions to milk and egg occurred in all targeted locations, particularly in relative houses and FE. Egg was the most common cause of reactions and those with milk allergy had the highest AAR of anaphylaxis to any identifiable allergen. Thus, the data in this study highlights the real-life, profound effect of these two allergies, albeit transient for most children. It is justification for ensuring all barriers to early introduction of baked products are removed and to encourage strong parental commitment with the current milk and egg tolerance models (iMAP Milk Ladder and IFAN egg ladder).

There are a number of limitations with the data reported in this chapter. As a third of reactions were due to unidentified reactions, there is a difficulty in calculating an accurate rate of annual reactions for known allergens. Some of these unidentified allergens may also have been new exposures, but as detailed above screening for these is not always appropriate.

We have mentioned that a proportion of participants had follow up for AARs during the first lockdown period of COVID-19 pandemic. The restrictions placed on people at this time do not reflect "normal circumstances". As detailed above calculating the potential effect of the lockdown on allergic risk is challenging

Although we reached our sample size required to report the overall incidence of AARs in the group as well as the overall rate in G2 (5-12 yr. olds), we did not reach the sample size required for either G1 or G3. This will be discussed in detail in chapter 6.

The information that we collected did not provide us with enough information to fully establish causation for each reaction. This is not unique to this study and is a difficult task to undertake.

Conclusions

The data presented in this chapter is an analysis of the first, prospective study to examine the frequency and circumstances of accidental allergic reactions in Irish children and adolescents. It presents data which challenges the perception of variable risk across locations. It uncovers the need for improved recognition and management of anaphylaxis even in patients of a tertiary allergy clinic. It exposes further, the burden of milk and egg allergy in the young and is evidential to promoting early tolerance to both allergens. It reveals the challenge of unidentified allergens in eateries. It demonstrates both commonality and dissimilarity with international experience, highlighting the relevance of local studies in this area.

Chapter 4: FOOD ALLERGY IN IRISH SCHOOLS AND CHILDCARE FACILITIES

Section 4.1: INTRODUCTION

Schools and childcare facilities have a responsibility to keep children safe. The Children's First act 2015 (177) requires organisations to make provisions to protect children and ensure their safety. The Disability Act 2005 (178) protects many children with chronic conditions, however there is no specific law protecting children with other medical conditions not causing disability (such as FA).

Entrusting others with the care of a food allergic child can be very stressful for parents. The child's first day at childcare or school may be the first time that the child has been away from the parent for any substantial period of time. In this chapter, we will explore the Irish school and childcare environment with regards to FA.

Irish schools and childcare services

Children spend a large proportion of their lives in school and/ or in day-care. This can range from 4 to over 10 hours/day. Children in Ireland start primary school at age 4-5 years and then secondary school at 12-13 years. In addition, the Early Childhood Care and Education (ECCE) Scheme provides early childhood care and education for all children (age 2-5 years) within preschools and Montessori. Under this programme, education is provided by the state, for 3 hours daily during the school year for 2-5 year old (179). Furthermore, 38% of children (0-12years) are in non-parental childcare (Table 4.1.1)(180). In Ireland, Preschool Childcare Services (CCS) is an umbrella term encompassing include pre-schools, play groups, day nurseries, crèches, childminders, and other similar services looking after more than 3 pre-school children (181). The Child Care Act 1991 provides for the regulation and inspection of these services by Tusla (The Child and Family Agency). Therefore the term "preschool CCS" will be used throughout this chapter to describe these services. Table 4.1.1 illustrates the different types of Irish preschool CCS.

Other childcare options in Ireland include childminders (caring for 3 or less children) in their home, nannies who care for children within the child's home as well as relatives (Table 4.2.2). Afterschool services provide childcare in a facility after the school day is finished.

Table 4.1.1: Structure of Irish Preschool Childcare services

| Service | Description |
|--|--|
| Nursery or creche | Full or parttime day care service (usually from 6 months old) |
| Montessori / preschool | Education under the ECCE scheme |
| Playschool | Sessional service for preschool children focused on play |
| Naíonraí | Playschool operating through the Irish language |
| Childminder | Care for children (4-5 children under 6yrs) in the minder's own home * |
| *Childminders caring for 3 or less children are not provided for by the Childcare Act and are not regulated. | |

(Source: Citizens Information and HSE, TUSLA)

Table 4.1.2: Types of childcare available in Ireland

| | Children (0-12yrs) % |
|--|-------------------------|
| Parent | 70 |
| Unpaid relative or family friend | 16 |
| Paid relative or family friend | 3 |
| Childminder/ au pair/ nanny | 10 |
| Creche/Montessori/playschool/afterschool | 13 |
| Other | 1 |
| | |

(Source: Central Statistics Office: Irish census data 2016)

We know that 4.45% of Irish 2-year-olds have a FA (3). Using census data (56), this equates to more than 9000 food allergic children aged 2 and under in Ireland. The minimum ratio in childcare settings for children aged 1-2.5yrs, is 1:5; among 20 2yr olds in preschool CCS ,there will be one FA child. In primary school classes (with children as young as 4 yrs old), there can be over 30 children under the care of one teacher. Most classrooms in primary school can expect to have at least one child with a food allergic child in it. These are very large numbers of children and highlight how ubiquitous FA is in the Irish childhood population.

Consumption of food in Irish schools and childcare services

In Ireland, children attending nurseries and childminders, for the most part, are given food which is cooked onsite. They may also bring food from home for snack time. Children who attend preschools and primary school, commonly bring their own food from home. Some may be offered milk which is provided by the service at breaktime. Delivering Equality of Opportunity in Schools (DEIS) which make up a small number of the total schools in Ireland, provide children

with a subsidised lunch which is provided by an outside catering company and is funded by the state (182). Whilst a substantial number of adolescents in secondary schools bring in their own food, many also eat food from school canteens which is prepared onsite. Other schools may permit older students to leave the premises at lunch to buy food in a local shop/food establishment. schools,

Of note, there are usually 2-3 episodes of food consumption in school (lunch and 2 breaks) and up to 5 episodes in preschool CCS . As well as these planned daily episodes of food consumption there may be many episodes unplanned e.g. birthday parties, bake sales, cultural holiday celebrations. This food is most commonly brought in from outside, usually from the child’s home; it may not be labelled particularly in the case of bake sales or parties.

Potential environmental risks for food allergic children in schools and childcare

It is therefore, not surprising, that there are a number of factors, if not adequately managed, that can contribute to a parent’s anxiety about their food allergic child attending school or preschool CCS (183) . Multiple episodes of food consumption, activities involving food and staff changeovers are just some of the environmental risks that could potentially increase their risk of having an AAR in this setting (184) (Table 4.1.3).

Anxiety in both parents and staff can result in exclusion of children from activities or separation from peers at mealtimes which is not ideal. Indeed, Polloni et al found that staff in schools had difficulty in guaranteeing full participation in extra-curricular activities to food-allergic students (185). As well as exclusion, children with FA are twice as likely to be bullied as children without FA (186) . There are at least 2 reported cases in the Irish media of food allergic children in Ireland being discriminated against because of their FA which resulted in their schools being fined (187, 188).

Table 4.1.3: Potential environmental risks to children within schools and preschool childcare

| |
|--|
| |
| Lack of supervision at mealtimes |
| Multiple meals/breaks throughout the day |
| Meals consumed indifferent places |
| Fresh (unlabelled food) +/- provided by outside company |
| Activities involving food e.g. crafts. Cooking, bake sales |
| Staff changeover/ new staff |

(Source: Sicherer SH, Furlong TJ, DeSimone J, Sampson HA. The US Peanut and Tree Nut Allergy Registry: characteristics of reactions in schools and day care. J Pediatr. 2001;138(4):560-5)

Management of food allergy within Irish schools and childcare services

The cornerstones of FA management in schools and preschool CCS (or in any setting) include (i) methods to prevent relevant exposure to allergens and (ii) plans to recognize and treat allergic reactions and anaphylaxis (189). They have also been identified as the 2 main deficiencies (189, 190). It is imperative there are measures in place to keep food allergic safe in these settings. Although rare, there are documented cases of fatalities secondary to food induced anaphylaxis in schools internationally and the inquest into these preventable events is often the impetus for change. In Australia since 2002, there has been five deaths due to food related anaphylaxis in schools, including a death in 2018. The inquests into these deaths have led to a more systematic approach to anaphylaxis in schools in Australia (191) as has been the case in other countries. Inquests into two deaths in the UK in schools over the last 4 years, highlighted the lack of staff training on FA and readily available adrenaline as being major contributing factors to the deaths (192, 193).

However, despite there being no official onus on facilities in Ireland, it is encouraging that there are attempts from a number of sources to increase awareness and knowledge on FA among staff in schools and childcare settings. Early Childhood Ireland (a membership organisation for childcare workers) have a guidance document which incorporates information on avoiding accidental consumption of allergens and advice on having antihistamine available in the facility within the EYS. An all-Ireland agency, "safefood", set up to promote awareness and knowledge of food safety on the island of Ireland, has an online FA training module aimed towards preschool staff (194). TUSLA (the Irish state child and family agency) recommend that EYS providers to review this module. However, there is no obligation to do so.

The situation within schools is no different. There exists no specific guidance document from the governing body over schools (The Department of Education) in Ireland. IFAN has evidence-based information specific for Irish school and childcare settings available on its website which parents can point schools towards (195).

Administration of emergency medication

There is no legal or contractual duty for a member of staff in a school or a preschool CCS to administer medication or supervise a student taking medication. It is therefore not unsurprising,

that the management of FA is ad hoc and is dependent on individual Irish schools and preschool CCS with no onus on facilities to record FA policies.

In 2017, the Human Medicines Regulations (UK) were amended to allow all schools to stock AAI devices without a prescription, for emergency use in children who are at risk of anaphylaxis in UK and Northern Ireland and a guidance document was written (196). There also exists a ‘stock epinephrine policy’ for schools in the USA. This is not the case for schools in Ireland, however, colleges, workplaces and sports venues are permitted to hold AAI (adrenaline auto-injectors) in Ireland, yet many remain unaware of this legislation.

In 2015, the then Minister for Health in Ireland, passed legislation to allow members of the public (such as teachers, childminders) to administer lifesaving medication including adrenaline. This is important, as very few schools in Ireland have a school nurse. There are 35 active members in the Irish Nurses and Midwives Organisation (INMO) designated as school nurses, many working part-time and predominantly based in fee-paying schools with boarders. This contrasts with other countries. In Finland, school nurses are found in all schools (ref). Schools in Great Britain usually have a school nurse among staff. The case is similar in the USA, with 95% of schools in the one American study having a school nurse on site (47).

However, although “allowed to administer”, there is no legal or contractual duty for a member of staff in a school or a childcare facility to administer medication or supervise a student taking medication. It is our experience that parents are asked to sign waivers that they will not sue an individual if they fail to administer medication. This is a very unsatisfactory situation.

Education on food allergy management in schools/preschool CCS provided in the allergy clinic

The educational session that is provided in the CHI allergy department provides parents and carers with a number of instructions regarding school and preschool CCS attendance.

1. A copy of the IFAN management plan is to be provided to the school
2. All food allergic children should have oral second-generation antihistamine available to them
3. All children who are prescribed adrenaline, keep 2 adrenaline autoinjectors (AAI) in school or childcare as recommended.
4. Parents and carers are provided with a letter for the school explaining that and signposting the school to detailed advice on the IFAN website how to treat an allergic reaction (see appendix Y for copy).
5. Parents and carers are then advised to arrange a meeting with educational staff and train them.

At the current time, there is neither a legal nor formal requirement for AAI training in Irish childcare or education environments. It has been reported, that some EYS receive training on FA by TUSLA .

Accidental allergic reactions in schools and preschool childcare services

Data from other countries shows that proportionately fewer reactions occur in schools (5-20% of all AARs) (13, 86, 128, 131, 139) compared to other non-home environments. This is despite the amount of time children spend within these services. To date, there is no Irish data on accidental allergic reactions (AAR) within school or preschool CCS environment.

As healthcare professionals caring for children with FA, we have a responsibility, alongside educators to safeguard children in these environments. To be able to effectively do this, we need to understand the current management of FA as well as the number of AARs occurring within these environments In Ireland

This chapter describes the school and preschool CCS data in ReAACT and has the following outcomes:

Primary outcomes

- I. to identify the attendance patterns at school and preschool CCS of FA children attending our clinic
- II. to report the rate of accidental allergic reactions in school and preschool CCS and their management.

Secondary outcomes

- (i) Identify the routine practice with regards to FA management and prevention of AARs both in school and preschool CSS facilities.

Section 4.2: LITERATURE REVIEW

Introduction

There is a paucity of Irish data in this area. There are, however, a number of papers on the topic in the literature, the results of which may not be fully translatable to our setting. The structure of schools and childcare settings differ considerably from country to country. E.g. age of children, whether food is served or brought in, whether a school nurse is present or if FA training is provided to staff. Some countries (e.g. Australia and Canada) have had fatal anaphylaxis cases in the school setting. Unfortunately, it is due to these fatalities that there has been a motivation to make changes to create a safer environment within schools. We can assume that is why there are a number of publications on the topic from these countries.

Methods

A literature review was done on this topic. A descriptive narrative of the results follows.

The following areas were reviewed:

- (i) Accidental allergic reactions in school and preschool CSS facilities
- (ii) FA management plans and policies
- (iii) School preparedness for allergic reactions: availability of adrenaline autoinjectors, staff training and education
- (iv) Food bans and restrictions in schools and childcare settings

Results

An international guidance document was published on the management of FA in schools earlier this year (8) . This publication is the first attempt to summarise all available evidence and make recommendations. It does emphasise that there is a need to adapt the recommendations to each country's local circumstances. In particular, they highlight the lack of high-level evidence in this area, a point which also needs to be considered in this review of the literature.

Firstly, we will look at the literature on AARs within schools and preschool CSS. This will allow us to see the size of the problem. We will then go on to examine the literature on FA management and treatment within these settings and then look at the evidence for training and staff education.

Accidental allergic reactions in schools and preschools

After the home setting, one of the next most common location where AARs are reported is within schools. Historically the numbers of AARs occurring in schools was higher. American data from 1998 reported 50% of AARs in peanut/tree nut allergic children occurred in school (134). This is substantially higher than more recent papers which report rates of between 5 and 20% (13, 16, 86, 120, 121, 136, 139, 197). Unfortunately, this rate of 50% continues to be quoted and justifiably provokes anxiety within parents. Of 4586 children (9mon- 19yrs) on an American nut allergy registry, 750 (16%) report ever having a reaction in school or day care. They obtained further information on 100 of these. They do not comment on whether these children consumed food prepared in school or brought it from home. A quarter of reactions were mild (half due to craft products). Baked goods/candy account for 75% of food ingestion. A UK based study reported that only 5% of AARs occurred in school (13). This small number could be explained by the fact that only nut reactions were recorded. In addition, as part of the management package in this study, schools received a training package incorporating avoidance advice and emergency medication training and emergency treatment plans, coordinated by local community paediatric nurses trained in allergy. This study also showed that among children with nut allergy, preschool children have less reported AARs in comparison to school aged children (13% vs 56% of total AARs).

An American paper from 2001, looked at all cause reaction rate in schools and preschools and found peanut and milk accounted for over 60% and peanut 29% of AARs (47) ; 59% were not allowed to eat any food which was not provided by their parents, 22% ate regular school food, and 19% were allowed to have some of the foods and snacks provided by the school.

There is some recent data on AARs specifically within nurseries and preschools in Japan. In this study, data was collected directly from the nurseries via a nationwide postal survey (198). This method may have led to an underestimate of AARs due to under recognition or an over estimation as non-allergic events may have been included. They describe a higher incidence in younger children (<1 year) and suggest this is because younger children are more likely to share food which was the cause in 12% of AARs requiring treatment (199). Milk was the most common allergen (34.5%, aOR 1.239 (1.142-1.346) $P < 0.0001$) in this preschool population. Data collected from parents of children attending an American allergy clinic also found milk to account for most preschool reactions (32%) .

School preparedness for allergic reactions

(i) Food allergy Management/ action plans

Waserman et al highlight that FA action or management plans (AAP) drawn up by a healthcare professional (HCP) should be provided for all food allergic children in schools and childcare (8). Failure to follow an AAP has been shown to be a cause of delayed treatment for reactions in school (184). These action plans should be specific to each child, detailing their allergies, emergency medication and plan to manage an allergic reaction. They are an important communication tool between parents, school and allergist (190). It is concerning, that a number of studies report that a variable proportion (15-79%) of FA children do not have an AAP in school (47, 200-202). Where one does it exists, it is, as recommended, most commonly given to the school by the parents (201, 203); parents report adherence to it (47). An individualised healthcare plan must be provided by law to all schools for all food allergic children in France since 2003 (204). These are written by the allergist or general practitioner and then checked by the school doctor in that jurisdiction. Although a step forward, the authors do highlight that the lack of standardisation across the plans is an issue. The availability of a doctor designated to a specific school area is very uncommon worldwide, so their model has limited applicability outside of France.

(ii) Food allergy school policies

The existence of FA policies in schools and childcare settings is inconsistent. Variation in practice exists both between countries and also within different states or jurisdictions in America, Australia, and Canada (191, 205). Schools in the UK are required to have policies to support pupils with medical conditions; however schools must develop their own FA policies which inevitably leads to discrepancies (206). Having a FA child in a school appears to increase the likelihood of having a policy. One UK study 2016 found 57% of the schools without pupils at risk of anaphylaxis did not have a protocol in place. In comparison 73% of schools with currently registered food allergic children did have a FA Policy (95% CI 67–79) ($P < 0.001$) (207).

In parts of Canada, public schools must comply with Sabrina's law, brought in following the death of a teenage girl in her first year of high school (208). Sabrina's law requires school boards to have a FA policy and students deemed at risk of anaphylaxis to have individualised allergy

plans. The effectiveness of this legislation was assessed in 2010 by comparing legislated (Ontario) and non-legislated provinces (Alberta, British Columbia, Newfoundland and Labrador, and Quebec), and found significant differences in school compliance with policy, staff awareness and capacity to effectively administer an AAI (205).

In one American study, schools with FA policies were 3.5 times more likely to require student individual action plans than schools with no guidelines or policies (OR 3.5, 1.00-12.2, P =0.05) (209).

All Australian states and territories have anaphylaxis policies and guidelines outlining anaphylaxis recognition and management in schools (191).

Food safety control policies have traditionally been oriented preferentially to microbiologic hazards. Ortiz-Menéndez et al highlight the need for a specific policy around allergen-free food preparation if the school cooks food for students (202). They surveyed 27 schools in Madrid all with their own kitchen and found only 27% had a written plan for allergen free food preparation.

As part of FA policy, having a person to lead on FA within the service appears important. In a large nationwide study of in excess of 15,000 nurseries and preschools in Japan, Yanagida et al found more AARs occurred in nurseries without a person accountable for FA (199) . Dupuis et also highlight this and suggest having FA leaders in schools who communicate consistent messages as well as supporting FA students (210).

When designing a FA policy, Sheetz et al emphasise the importance of involving all stakeholders, and (211) and Sicherer highlights the key role allergists play in successfully mediate a reasonable evidence-based plan that promotes safety (189) .Children and their parents in a Canadian study, have reported feeling stigmatised as a result of overly protective school policies (212). To promote socialization, avoidance measures should minimize separation of children with food allergies from their peers.

It must be remembered that there is no evidence, that the existence of FA policies in schools reduces AARs. However this may be because these policies are not standardised. A school policy is worthless in isolation. It must be accompanied by the training of education of school staff on AAR prevention and management (8, 189, 190, 204).

(ii) Availability of adrenaline autoinjectors

Any child who has adrenaline autoinjectors (AAIs) prescribed for them should have adrenaline available to them at all times, including while they are in school or childcare. There is a large variation in the numbers of eligible children whose adrenaline accompanies them in school. A review of French schools (interviews with school principals and school doctors), found that of those with a child with FA, only 32% of the schools emergency kits contained adrenaline (204). An American study of AARs schools /preschools of children attending an allergy clinic, found 81% of parents provided at least 1 AAI (47). This large variation in numbers may be due to the source of selection of eligible patients with higher number carrying AAIs in those recruited from allergy clinics. These studies predate the availability of stock adrenaline in some countries (discussed below).

There also appears to be a variation in where adrenaline is located. In the French study they were stored in the classroom (33%), the nursery (14%), or the principal's office (10%) (204), whereas an American study reported that adrenaline was kept in a nurse's room for 58%, in the classroom for 28%, and in the front office for 18% of children; 17% of the children (median age 6.6 yrs) carried their medications with them (47). The same study reported on the location of adrenaline in preschools, classroom in 48%, in the front office in 43%, and in the kitchen in 14%, with 5% of the preschools having medications for the treatment of food-allergic reactions available in more than 1 location (47). A Canadian study reported, that among the children (mean age 8.1 yrs), 48% carried their own AAIs; of those who did not, it was stored in the majority (78%) the nurse's office (213). It is recommended that if there are 2 AAIs in school for the child, that they are stored together. However, one study found in 30% of cases they were stored in different locations . (214).

Of course, as children get older, they can take responsibility for their AAIs and carry them on their person. In one study, 70% (95% [CI], 50.6%–85.3%) of those aged 5 or 6 years, 43.8% (95% CI, 31.4%–56.7%) aged 6 or 7 years did not carry their own AAI (213). These are quite high numbers of young children taking responsibility for carriage of their AAI which does not seem appropriate. When discussing readiness for students to self-carry and self-administer adrenaline in school, Hui et al recommend that this determination is not based on age alone. Instead, both the clinician and caregiver should assess how capable the child is in recognizing symptoms, correctly using adrenaline, and how comfortable the child feels with assuming this responsibility (203). It should not be left for the school to decide. Abrams suggests this decision should be

made by the families and schools should support this approach and not insist upon locking the device in a school office (215) .

A number of countries (including USA, Australia, UK) have “stock” AAls in the school. Previous studies have found 20-24% of allergic reactions in schools were in children who had no previous history of allergy (214, 216). These children particularly benefit from the availability of these AAls. After Australia passed legislation to allow a supply of AAls in schools, there was a documented improvement in management of allergic reactions (191). Similar legislation exists in the USA. In 2016, legislation was introduced in the UK, to allow schools to purchase “generic” or “spare” AAls (217). However, no funding was provided to schools to pay for these or to train staff (206). A recent metanalysis reported that the provision of stock adrenaline in schools to be cost effective (218).

(iv) Education and Training of staff on food allergy

AAls are not used frequently in schools. Two public health reports from Massachusetts, USA reported that adrenaline was administered in 6% to 7% of schools over the course of a year (219, 220). However, it must be remembered that reported rates of adrenaline use might not represent the rates at which adrenaline is medically indicated. In some cases, adrenaline might not have been used to treat anaphylaxis when it should have been. In other cases, adrenaline might have been used to treat an allergic reaction that did not meet the criteria for anaphylaxis.

Both knowledge of and training in FA among school staff is not well reported in the literature. In one UK study of schools, only 47% of the respondents (95% CI, 39-57%) felt confident to manage anaphylaxis (207). Training of all school personnel is crucial because response time is one of the main factors implicated in the severity of anaphylaxis and risk of death (221). Sicherer also showed that treatment delays were attributed to delayed recognition of reactions, calling parents and an unsuccessful attempt to administer adrenaline (184). The literature is in agreement that the contents of the training should be overseen by healthcare professionals expert in allergy (8, 184).

There are, however, a number of suggested methods on how this training is/might be delivered. Incorporating a FA training curriculum for childcare workers into training conferences has been shown to be successful at increasing FA knowledge (222). Higgs et al reports on the development of a Whole School (WS) Food Allergy Awareness Toolkit for UK secondary schools which reduced reactions and increased societal acceptance of FA within the schools (223). An Italian group has evolved The Food Allergy Community programme which incorporates a series of short videos to

educate school and restaurant staff on FA (224) , the effectiveness of which is unknown/unpublished. When seeking to understand the effectiveness of educational interventions in school, we can look beyond allergy. A Cochrane review concluded that there is insufficient evidence that school-based educational programmes can prevent unintentional injuries (225). Clearly further research is needed.

(V) Food bans and restrictions in schools and childcare settings

In an effort to reduce the risk of AARs, many childcare facilities and schools have implemented food bans. Others prohibit food in certain areas e.g. nut free classroom. Indeed, food bans within schools and childcare are not endorsed by governments or allergy organisations and some such as the Australasian Society of Clinical Immunology and Allergy (ASCIA), specifically advise against it (226).

So why are these facilities banning specific foods? Greenhawt highlights that the idea to ban food (in particular peanut) has arisen from misconceptions about the risk of reaction and route of exposures; many are unaware that severe reactions require ingestion of food (peanut) and no evidence exists that reactions occur to inhaled peanut (215). Another factor encouraging bans, stems from misperception of the potential risk of fatal anaphylaxis (215) which is an exceedingly rare event in children.

It must be noted that most of the research done on food bans is related to nut, in particular peanut. However most of the cases of fatal anaphylaxis in children are due to cow's milk. A 10-year UK retrospective review of paediatric anaphylaxis fatalities found incidence of 0.006 deaths per 100,000 children per year, with milk having caused 50% of those deaths (227). In addition, with milk resulting in a number of AARs within schools/preschools (47), it might be more useful to focus on its avoidance rather than indiscriminate bans of nuts.

How many schools actually ban foods? In one Canadian study, 71% of schools prohibited peanut (146). An Australian report found 30% of schools were banning nuts despite the recommendation by ASCIA against banning. An American study of 1430 school nurses found that 66.5% of schools had allergen bans in classrooms and 31% of schools had a school-wide allergen ban (228).

Bartnikas et al highlight that there is this variation in food ban school policies within even within one state- Massachusetts; They showed that none of the food bans appear to completely exclude allergic reactions, although schools with peanut-free tables had lower rates of

adrenaline administration (19). Other studies concur with these findings and conclude there is no available evidence that interventions which ban certain foods in schools lower the risk of allergic reactions (16, 28) or improve quality of life (229). A Canadian allergy cohort study of 567 accidental exposures in 429 allergic children (over 4589 patient-years) showed more reactions at schools/day care centres that prohibited peanut than at those that allowed it (4.9% [95% CI 3.3–7.1] vs 3.0% [95% CI 1.8, 4.8], respectively) (18).

In addition, other studies have found that it can be challenging to effectively monitor these restrictions and prohibitions. Some students still bring prohibited foods to school (230) and allergic reactions still occur in schools where a food (peanut) is prohibited (16, 18, 231). In addition, Wasserman suggests that these restrictions might limit the development of self-management and social skills in students with FA, which might reduce their preparedness for settings where their allergens are not prohibited (8). Peanut bans may send a message to a child and caregiver that any environmental peanut exposure is dangerous (215). Another inadvertent result of food bans could be decreased school preparedness to treat anaphylaxis. Abrams et al found a lack of school preparedness to manage allergic reactions at schools with food bans, including failings in recognizing and treating allergic reactions (215).

But is there any evidence for the banning of food? Wasserman et al's suggestion may not be suitable for all environments particularly when young children are present. e.g. young children may need restrictions in place as they lack the awareness to avoid or share foods and often put food in their mouths (232). Kato highlights that infants and toddlers "eat each other's food" with children eating spilt food or food from other children's trays as unique but common cause of allergic reactions within preschools (233).

Conclusion

Allergic reactions do occur in schools and preschools. There are a number of measures that can be put in place with the aim to keep children safe, each with varying benefit. The evidence for banning foods or having standardised protocols without appropriate training is low and doesn't seem to affect the risk to the child. It appears the emphasis should be placed on recognising and effectively managing allergic reactions in the school and childcare setting with the help of action plans. The approach should be one of collaboration between the school, the parent and the allergist who all have the safety of the child as a common goal.

Section 4.3: METHODS

The methods sections in chapter 1 (Section 1.3) and in chapter 3 (Section 3.3) describe all relevant methods for this chapter. Of note as discussed in the introduction: the term preschool childcare service (CCS) includes pre-schools, play schools, nurseries, crèches, childminders, and other similar services looking after more than 3 pre-school children (234).

Section 4.4: RESULTS

The majority of participants in ReAACT (n=519, 98%) were attending some form of schooling or preschool CCS.

Children attending each facility

402 of the 531 participants in ReAACT, attended school (317 primary school, 85 secondary school). No children were home-schooled. 42 (13.2%) primary school attendees also attended an afterschool facility. The median number of children in a primary school class was 28 (LQ 27, UQ30). The majority of children travelled by car to school (n=300, 75%). Very small numbers took school bus (n=30, 7.5%), walked with friends (n=28, 7%), =)walked with parent (n=22,5.5%), public transport (n=19, 4.7%), walked solo (n=6, 1.5%).

There were 119 children attending preschool CCS; of which, 67 children attended preschool and 50 children attended nursery. Of those attending preschool, 12 had another form of childcare (childminder (n=7), nanny (n=3) relatives (n=2)) (Table 4.1). 10 children (age 2-4 years) were cared for at home by their parents. The median ratio of children to staff in creches was 1:5 (LQ 1:3, UQ 1:8) and in preschool was 1:10 (LQ 1:4, UQ 1:15).

Overall, there was a small proportion of children looked after by a childminder (4.3%), Nanny (2.2%) or a relative (1.9%) on a regular basis. (Table 4.4.1). The majority of participants (85%) relied on relatives for ad hoc childcare.

Table 4.4.1: Breakdown of attendance at school and childcare services

| Type of school or childcare | N (%) |
|---|------------|
| Schools | |
| Total in school | 402 |
| Primary school | 317 (59.7) |
| Secondary school | 85 (16) |
| Afterschool facility | 42(13.2)* |
| Preschool childcare services | |
| Total in preschool childcare services | 119 |
| Preschool/ Montessori | 67(51.9)** |
| Nursery | 50(38.7)** |
| Childminder (4-5 children) | 5(3.9)** |
| Other childcare services | |
| Childminder (3 or less children) | 18(3.4) |
| Nanny | 12(2.2) |
| Relative | 10(1.9) |
| Of note, there was overlap between some categories e.g. some children attended both childminder and preschool and others were in school and had a nanny. *The denominator is primary school aged children (n=317) ** The denominator is preschool aged children (n=129) | |

Availability of allergy management plans and policies

323 (60.8%) of these educational and childcare facilities had a food allergy policy (FAP) in place that the parents were aware of. Compared to preschool CSS and primary schools, secondary schools were less likely to have a FAP in place (RR 0.70, 95% CI 0.54-0.90, P=0.0058). Two thirds (66%) of parents had provided the service with an allergy action plan (AAP) and this proportion was similar across all facilities (Table 4.4.2).

Adrenaline autoinjectors

Overall, 510 of participants (98%) had 2 AAIs available to them in each facility, but in 35% of cases the two devices were stored in separate locations. Just under a quarter (23.5%) of adolescents carried their own AAIs in school. The commonest locations for AAI storage in primary schools were teacher’s desk (n=82, 20%), classroom (n=83, 20%), office (n=75, 18%).child’s bag (n= 71, 17%), In 16% of cases the location of AAI in school was unknown by parents. The commonest locations for

AAI storage in preschool CSS were the classroom (n=44, 38%), child's bag (n=29, 25%), office (n=9, 7.8%). A similar proportion of parents did not know where the AAI was located in the preschool CSS (18%) as compared to schools.

Restrictions and food bans

There were no cases of food allergic children eating in separate rooms from their peers. There were 4 children identified (2 in preschool and 2 in primary school), however, who ate at separate tables to their peers. Overall, 74% (n=398) of the facilities banned nuts. In 45 (8.4%), the ban was limited to the classroom of the allergic child. A larger number of preschool CSS (n=105,90%) banned nuts when compared to secondary schools (n=32, 37%), (RR 2.34 95% CI 1.76 -3.10, P<0.0001) and primary schools (n=247, 78%), (RR 1.13 95% 1.0371 to 1.23 , P=0.0056). A quarter of creches/preschool also banned another food (raw or lightly cooked hen's egg, kiwi, sesame, fish).

Food available within the facility

The source of food consumed varied across facilities (Table 4.2). 89% of children in the study reported bringing food from home to eat. Very small numbers of primary schools distributed food on a regular basis (n=30, 9.4%). Most just distributed fruit and milk but 3 (2.5%) primary school facilities providing food by an outside catering company. In contrast, 77% of secondary schools attended by allergic adolescents had a canteen providing food. Likewise, almost half of creches/preschools provided food.

Food Consumption within the facility

Regular: Only 25% of overall participants exclusively ate food prepared at home. Facility prepared food was regularly eaten by 35% of those in preschool CCS and 50.5% of those in secondary schools.

Ad hoc: Parents were also asked whether their child would on occasion, consume food brought into the facility by another child or teacher. According to their parents, 83% of secondary school adolescents did, 72% of primary school children did and 38% of preschool/creche would accept food brought in by teachers and other students. In 38% of preschool/creche children and 28% of primary school children, parents considered that the teacher would communicate with the parent prior to giving the child food brought in by another child or themselves.

Table 4.4.2: Characteristics of food allergy management within each facility

| | Overall N= 521 | Preschool CSS N= 119 (23%) | Primary school N=317 (61%) | Secondary school N= 85 (16%) |
|---|---------------------------|---------------------------------------|---|---|
| FA policy n(%) | 308 (59) | 61 (51) | 210 (66) | 37 (43.5) |
| Copy of AAP n(%) | 346 (66.6) | 79 (66) | 210 (66) | 57 (67) |
| AAIs brought to facility n(%) | 511 (98) | 116 (98) | 313 (99) | 82 (96) |
| AAI stored together n(%) | 339 (65) | 78 (66) | 205 (66) | 56 (65) |
| Carry own AAI n(%) | 25 (4.9) | 0 | 5 (1.6) | 20 (23.5) |
| Nut-free facility n(%) | 386 (74) | 107 (90) | 247 (78) | 32 (37) |
| Bring food in from home n(%) | 466 (89) | 106 (90) | 283 (89) | 77(90) |
| Food made on site/ catered n(%) | 149 (28.5) | 55 (46) | 30 (9.4) | 64 (77) |
| Food made onsite consumed by child n(%) | 106 (20) | 42 (35) | 21 (6.6) | 43 (50.5) |
| Eat food brought in by others n(%) | 346 (66) | 45 (38) | 230 (72) | 71 (83) |
| Abbreviations: AAP: allergy action plan; AAI: adrenaline autoinjector; CCS: childcare services; FA: food allergy; | | | | |

Accidental allergic reactions in schools and childcare

The school environment was the third most common site of overall AAR occurrence (n=18/220, 8.2%). Less again occurred in preschool CSS (n=6, 2.7%).

Schools:

Eighteen (12%) of the 149 reactions, in school-aged children (4-5yrs- 16yrs in ReAACT) occurred at school. School aged children were more likely to react at home than at school (RR 4.77, 95% CI 2.93-7.78, P<0.0001). The annualised incidence of AARs in school was 4.5% (95% CI 2.6-7.0). Primary school aged children (5-12 yrs, n=16) were twice as likely to react compared to adolescents (13-16yrs, n=2), RR 2.1 (95% CI 0.50-9.1, p=0.3).

The main allergens implicated were unidentified nut (n=4) hen's egg (n=4), tree nut (n=2), cow's milk (n=2), peanut (n=1). In 5 reactions, the allergen was unidentified. Six of the 7 reactions known to be caused by a nut occurred in schools where nuts were banned.

(56%) reactions were caused by allergen ingestion and 4 were graded as anaphylaxis. All 4 anaphylactic reactions occurred in primary school aged children with 3 receiving adrenaline but none by school staff (2 by parent when called to school, 1 by emergency department staff) (Table 4.4.4); Regarding overall treatment, 17 were administered antihistamine (5 by school staff). Table 4.4.3 provides the full details of these 18 reactions.

Table 4.4.3 Details of accidental allergic reactions occurring in schools

| Reaction description | N |
|--|----|
| Causative allergen | |
| Unidentified allergen | 5 |
| Unidentified nut | 4 |
| Tree nut | 2 |
| Egg | 4 |
| Cow's milk | 2 |
| Peanut | 1 |
| Type of exposure | |
| Ingestion | 10 |
| Contact | 7 |
| unknown | 1 |
| Source of food | |
| Friends lunch | 7 |
| School event (bake sale/party/treat day/pancake Tuesday) | 7 |
| Brought from home | 2 |
| Unknown | 2 |
| Severity | |
| Non-anaphylaxis | 14 |
| Anaphylaxis | 4 |
| Cause of reaction | |
| Accident/human error | 8 |
| Did not read ingredients | 4 |
| Did read ingredients/ Possible cross contamination | 4 |
| Unsure | 1 |
| Treatment received | |
| Antihistamine | 17 |
| Adrenaline autoinjector | 3 |
| Inhaled bronchodilator | 2 |
| None | 0 |
| Person administering adrenaline | |
| Parent | 2 |
| Teacher | 0 |
| Healthcare professional in hospital | 1 |
| Hospital treatment | 4 |

Table 4.4.4 Description of the 4 anaphylaxis reactions in school

| | Case 1 | Case 2 | Case 3 | Case 4 |
|---|---------------|---|---------------|---|
| Age (yrs) | 12 | 4 | 10 | 8 |
| FAP in place | N | N | Y | Y |
| AAP in school | N | N | N | Y |
| AAIs location | Schoolbag | Unknown | Unknown | Office |
| Culprit allergen | Peanut | Unidentified (Allergic to hen's egg, cashew, pistachio) | Cashew nut | Unidentified (Allergic to peanut, cashew, hazelnut) |
| AAI administered by school staff | N | N | N | N |
| AH administered by school staff | N | N | Y | N |

Abbreviations: AAP: allergy action plan; AAIs: adrenaline autoinjectors; AH antihistamine; FAP: food allergy policy; N:No; Y: Yes.

Preschool CCS:

Six reactions occurred among children who attended preschool CSS (Table 4.5). Therefore, the annualised rate of reaction in preschool CSS was 5% (95% CI 1.8-11.1). No more than 1 reaction occurred at each site. Five were due to ingestion and one was graded as anaphylaxis. The implicated allergen in 50% was cow's milk and in 2 cases the allergen was unknown including the anaphylactic reaction. A detailed interview with the parents of the young child failed to identify the trigger. The child was known to be allergic to both egg and nut and tolerant of cow's milk. No accidental reactions to nut were recorded in preschool CCS.

Three of the facilities, where reactions occurred, had a FAP on site according to parental report. The parents of 2 of the children had provided the service with an AAP. In the case of the child who experienced anaphylaxis,(number 6 in table 4.4.5), the mother of the child was called to the nursery to collect her child and did consider administering adrenaline but chose not to. All children were administered antihistamine (3 by the staff in the preschool CSS).

Other childcare options

No reactions occurred while children were being cared for by childminders (3 or less children) or a nanny. There were 4 reactions while children were being cared for by relatives (all unplanned). In 2 cases, the label was not read and in 2 cases the allergen was given to the child accidentally. None of these reactions were severe (3 mild, 1 moderate).

Table 4.4.5 Reactions within preschool childcare services

| | Age (yrs) | Causative food (allergen) | Type of exposure | Circumstances | Severity of reaction /symptoms | Treatment |
|---|-----------|--------------------------------------|------------------|---|--------------------------------|-----------|
| 1 | 3 | Cheese (cow's milk) | I | Child given cheese and crackers at snack time (Failure to follow basic procedure) | mild | AH, INH |
| 2 | 2 | Pancake (egg) | I | Pancake Tuesday (Failure to risk assess play activity) | mild | AH |
| 3 | 2 | Cereal (unknown) | I | Child given wrong breakfast cereal (Failure to follow basic procedure) | mild | AH |
| 4 | 2 | Bread (cow's milk) | I | Staff member brought in fresh bread from bakery to share with children (Failure to read ingredients) | mild | AH |
| 5 | 2 | Playdough (cow's milk) | C | Play activity (Failure to risk assess play activity) | mild | AH |
| 6 | 4 | Composite meal - breakfast (unknown) | I | New staff member (Failure to assess risk of new staff) | Severe | AH |

Abbreviations: C: contact; I: ingestion; AH: antihistamine; INH: salbutamol inhaler

Associated factors

There was a lower number of FAP in schools where children had a reaction (n=10, 55%) when compared to those where there was no reaction (n=247, 61%), but this did not reach significance (RR 0.80, 95% CI 0.35-1.78, P=0.613) (Table 4.4.6). A higher number of children with AARs graded as mild had AAPs in place in school as compared to those who had anaphylaxis (OR 1.66, 95% CI 0.13-20.5, P=0.69).

Children with an AAP in their school or preschool CSS had a significantly lower risk of an AAR when compared to those without (RR 0.2, 95% CI 0.09-0.47, P=0.0002) (Table 4.6). There were more AARs in children who consumed food made on site (RR 1.75, 95% CI 0.74-4.11, p=0.195) and in those who consumed food brought in by others (RR 2.13, 95% CI 0.86-5.26, p=0.100).

Table 4.4.6: Associated factors for reactions in schools and preschool childcare services

| | Reaction N=24 (5%) | No reaction N= 497 (95%) | RR | 95% CI | P value |
|--------------------------------------|-------------------------------|-------------------------------------|-----------|---------------|----------------|
| Nut free facility | 18 | 368 | 1.04 | 0.42-2.58 | 0.916 |
| FAP | 13 | 295 | 0.80 | 0.35-1.78 | 0.613 |
| AAP | 8 | 338 | 0.20 | 0.09-0.47 | 0.0002 |
| Food made on site in facility | 8 | 141 | 1.24 | 0.54-2.85 | 0.526 |
| Consumed food made on site | 7 | 99 | 1.61 | 0.68-3.78 | 0.271 |
| Consumed only food brought from home | 5 | 127 | 0.78 | 0.29-2.05 | 0.620 |
| Consumed food brought in by others | 18 | 328 | 1.51 | 0.61-3.75 | 0.367 |

Abbreviations: AAP: allergy action plan; AAR: accidental allergic reaction; CI: confidence interval; FAP: food allergy policy.

Section 4.5: DISCUSSION

This chapter provides important and novel data on FA management within the school and preschool setting in Ireland, in a cohort of infants and children for whom diagnosis is confirmed and recommendations provided. Data from ReAACT demonstrates that the majority (98%) of this representative food allergic cohort are attending either preschool CCS or school services.

Accidental allergic reactions in school

School was the 3rd most common site for AAR occurrence after home and FE; 12% of AARs recorded in school aged children occurred in school. We show that school aged children are significantly more likely to react at home than at school (RR 4.77, 95% CI 2.93-7.78, P<0.0001). This is comparable with other studies, where reactions in school are less frequent than at home (16, 17, 120, 144). The number of AARs occurring in school in ReAACT is lower than a UK study by Uguz et al which reported that one fifth of children reported a reaction (to any food) in school or day-care in the previous 6 months (139). Yet, it is higher than another UK based prospective study which reported that 5% of AARs occurred in schools (13); However, the study design differs from our study in that only reactions to nuts were recorded. Furthermore, notification to the schools of the FA and provision of education and training to schools via community nurses were part of the study design. An international survey (recruited participants online from mostly north America) found 18% of children's most recent reaction occurred in school (14). Almost a quarter of school related AARs reported in our study were severe which is comparable with previous work by Sicherer et al (19%) (184).

Accidental allergic reactions in Preschool childcare services

8.5% of AARs in children who attended preschool CCS occurred within these facilities. Direct comparison with other studies is difficult; Some studies do not separate out school and day-care reactions as in this study (14, 18). Not all studies recorded reactions to all allergens as was done in ReAACT, e.g. a Canadian study which only recorded incidence of peanut reactions, reported 3.8% occurred in a day-care setting. Another study of milk allergic children (median age 32 mths) found 19% of AARs occurred in day-care (144). Fleischer et al reported a much higher reaction rate of 0.81 in their 5yr multicentre study of preschool AAR (132). However, their study included

infants from 3 months of age. Our study excluded infants below 2yrs as it is common for atopic infants with milk and egg allergy to have frequent non-specific contact reactions and eczematous flares which risks overinterpretation.

Studies also differ in their definition of day-care. In our study we applied national definitions (181) and analysed reaction data separately for those subject to regulation by TUSLA and those that were not (child minders <3 children, nannies and relatives). All reactions were reported in regulated childcare facilities, with no reactions recorded for children cared for by childminders (<3 children) or by nannies.

Our study reveals that reactions to cow's milk is a risk for young children attending preschool CCS in Ireland. Cow's milk (CM) was the implicated allergen in 3 of the 6 (50%) preschool CCS reactions. Other studies also report high level of CM reactions in preschool settings, 34% (235), 60% (47) , (42.3%) (132). These higher number of AARS to CM in young children compared with school going children are not entirely unexpected; the natural history is that milk allergy is outgrown (92% by 5 years) (236). Boyano et al specifically looked at AARs within children with milk allergy and found that 19% of them had a reaction in day-care (144). CM allergy may be "a wolf in a sheep's clothing" to those unfamiliar with FA; it may not be taken as seriously as nut allergy or confused with lactose intolerance (237); however CM is the leading cause of fatal anaphylaxis in children (238).

"Causes" of allergic reactions

As already discussed in chapter 3, behind every accident (or in this case, allergic reaction) there lies numerous contributing factors, causes and sub-causes (239). In the preschool CCS all but 1 of the recorded reactions involved ingestion. It is likely that allergic children were having mild transient contact reactions with allergens that went unnoticed. Contact reactions are harder to prevent than ingestion and less likely to cause significant reactions. AAR prevention should be focused primarily on prevention of accidental ingestion. In this study, an attempt was made to identify at least one of the primary causes for the AARs through interview with the parents of the child. It appears that all of the AARs occurring in preschool CCS could have been avoided if staff had followed basic procedures such as reading ingredients, considering the risk of play activities and educating new staff. A third of children in preschool CCS were allowed to eat food brought into the facility by others. Food consumed at breakfast time resulted in 2/6 reactions in preschool CCS. Although, these are small numbers, there are a number of potential reasons why this time of the day may be a higher risk time. Breakfast food is provided by the facility; other children are being dropped off concurrently, leading to distraction of staff; staff often have staggered start

times with the result there is limited supervision at this time. Identification of these small details is critical to the development of future safety policies.

That is as far as we can comment as the study was not designed to perform/access results of incident investigations. Although errors made by specific individuals can result in an event, there may be organisational factors within which an individual operates, which make the error more likely to happen. This has found to be the case in major accidents (240, 241), but the same principle holds true for smaller accidents. Education of staff on label reading in conjunction with basic procedures for staff to follow when serving food would potentially prevent similar reactions occurring again. However it is likely that a more complex training model is required. A specific multidisciplinary training course (2hours long, conducted by an allergist, a psychologist, and a lawyer) has been shown to be effective at improving school staffs' self-efficacy in managing FA and anaphylaxis (242).

Our study concurs with international data that widespread nut bans do not result in fewer reactions (27, 28). Six of the 7 recorded occurrences of accidental nut ingestion in schools happened in those that banned nuts on the premises. This risk of a reaction was not decreased in schools that were designated "nut free" (RR1.04, 95% CI 0.42-2.57, p=0.925). Only 25% of children exclusively ate food prepared at home. This is lower than data from an American study which reported 59% only ate food provided by parent (47). This study is 20 years old, but there is no more recent comparable data. Reassuringly, formally prepared school food from canteens was not the source of the reactions in secondary schools. AARs in schools, for the most part, occurred due to the child taking food from another child or ingesting food brought in for occasional events such as birthday parties. The majority of parents of primary and secondary school going parents were aware that their children, at times took food from teachers and other children. Over 1/4 assumed that this was fully supervised. However, it appears that a break to a routine such as either with a celebration or a new staff member clearly represents a high-risk time. Sicherer also found a quarter of school/day-care reactions occurred when there was an interruption to routine (8) . This point is further highlighted by the fact that most of the AARs occurring in relatives houses in ReAACT occurred during unplanned care of children by a relative.

In the authors opinion, the widespread use of nut bans in Irish schools is representative of lack of central policy and national guidance for school boards. The data shown here indicates that in the future Irish school FA policies should be focused on limiting the sharing of food in school through education, increased supervision and discouraging the use of food for treats and celebrations.

However, sharing of food will not prevent all reactions as data from this study shows that 2 of 18 reactions in school occurred due to errors made in home preparation of food.

Accidental allergic reaction preparedness

The annualised risk of reaction was 4.5% in schools and 5% in preschool CCS and the overall rate of anaphylaxis was 0.9%. These are very large numbers of children; we can expect 1 in 20 Irish food allergic children to have an AAR of any severity and 1 in 110 to have anaphylaxis in the facility they attend each year. This underlines the necessity that schools and preschool CCS are prepared for such events. Key components to preparation should include a FAP, Allergy management plans for all allergic children and easy access to AAIIs.

1. Food allergy policy

In this study it was demonstrated that less than two thirds of schools had a FAP, as reported by parents. The particularly low number in secondary schools (43%) might indicate that they do not consider FA their responsibility, but the responsibility of the teenager. Within a UK survey of schools, a slightly higher number (76%) of schools had FA management plans (243). Our findings are quite different from countries where legislation exists to ensure all schools have a FA policy in place e.g. Canada (208), Australia (226) and France (204). An FAP not only provides guidance for staff but also can be a source of information. In ReAACT, a third of AARs occurring in school were caused by cutaneous contact with the allergen and were not ingested (all were graded mild). 26% of reactions in Sicherer's report of AARs in schools, also occurred due to contact. This potentially reflects a lack of awareness of school staff on the risk of reaction by skin contact with an allergen. Mechanisms on how to avoid allergens and prevent of cross-contact should be included within a FAP. This is highlighted in the recently published "Model policy for allergy management at school" document by the British Society of Allergy and Clinical Immunology (BSACI) and partners and is discussed in more detail below.

2. Allergy management plans

Despite the study cohort all attending a tertiary allergy centre and received a personalised allergy management plan, 34% of parents did not provide the school/preschool CCS with an AAP. Analysis of the data collected reveals that children with an AAP had a significantly lower risk of an AAR as compared to those without (RR 0.2, 95% CI 0.09-0.47, p=0.0002). Our findings are mirrored in the literature. Previous studies from a range of countries report rates of 15-79% of children without an AAP in school (47, 201, 202). There is one piece of previous Irish data in this

area- a survey of Irish preschools in the West of Ireland; this found that 53% did not have AAPs (244). However, this study does not report how many attended an allergy service.

3. Adrenaline autoinjectors

Almost all (98%) participants prescribed adrenaline autoinjectors (AAIs) brought them into school; However, only a small number are carrying their own AAIs (only 24% of adolescents). This contrasts with Canadian data -with 64% of adolescents carrying their own AAIs in school. Canadian legislation ensures policies are in place in schools which guide best practice. The age at which a child is ready to carry their own AAI is dependent on the individual, it should not be determined by age (203). It is a decision best made by the child and their family, supported by their HCP and should not be left up to a school to decide (215). AAIs were reported to be stored in 1 or 2 of 7 locations throughout the school. This represents a risk, as staff may not be aware where to find a particular child's AAI during a reaction. This question of accessibility has been previously been highlighted by Pouessel et al. They found that AAIs were in one of 3 locations and half of them were under lock and key (204).

Response to accidental allergic reactions

Four of the 18 school reactions met the criteria for anaphylaxis, but no child received emergency treatment with adrenaline by a school staff member. In 2 cases the parents administered it on arrival to the school. Indeed, among the 17/18 who received antihistamine, in only 5 cases, did a school staff member administer it. This was despite the AAR being recognised by school staff. The rate of AAI administration in schools is variable worldwide. In one retrospective study from the USA, all 6 cases of anaphylaxis were treated with adrenaline given by either a teacher or school nurse (47). Another American review of school reactions found only 33% of those with severe reactions secondary to food ingestion were given adrenaline (231). Even with legislation and FA policies in place, AAI may not be used when appropriate in school. Loke et al found that despite increasing prevalence of anaphylaxis risk and AAI prescription in children attending schools in Victoria, Australia, that AAI activation has remained fairly stable (245). The authors consider that this may reflect the failure to use such devices when required or that strict risk minimization strategies in school have limited accidental exposure and reactions to allergens, or both. Schools staff consider themselves ill prepared to manage an AAR; 81% of schools in a UK survey felt that further training was needed while the majority stated that face-to-face training was preferable (243)

Recommendations

The information we have collected in ReAACT provides us with a huge opportunity to improve FA management within Irish school and childcare CCS. The value of this study is that it provides local information, collected from a cohort of children whose experiences are representative of FA allergic children nationwide in this small country. Freedom of Information data obtained by IFAN, states that the Department of Education has not reports of food allergic reactions occurring in schools. This study information can now be used to lobby for and to inform the designing of a national schools policy on the care of Irish food allergic children that includes all members the school team.

For now:

This study has highlighted the need to for us as clinicians to emphasise to parents the need to communicate with schools and preschool CCS. Parents should be advised and reminded at clinic appointment to provide their school or preschool CCS with an AAP on a yearly basis. This provides an opportunity to educate the school staff on FA and identify and mitigate potential risks to the child. As allergists, we need to support parents in communicating with the school and preschool CCS. Written advice should be given on common pitfalls within these environments. A video of a parent communicating information to a school staff member could be provided.

For the future:

- 1. Introduction of standardised FAP in schools and preschool CCS*

A collaborative approach between healthcare professionals and education governing bodies is required. The UK has recently published a “model policy for allergy management at school” document. Allergy advocacy groups, the BSACI (HCPS) and the Department of education all contributed to this guideline which includes an example of a comprehensive working FA policy. This guide is designed to support schools to develop a ‘Gold Standard’ FAP to manage children’s allergies safely. A similar approach could be adopted here, between the department of education, IFAN and relevant school and preschool CCS bodies. A government policy in this area is required and this Irish data supports this.

2. *Stock adrenaline autoinjectors in schools*

This has been shown to be cost effective in other countries (218)

3. *Education and training on FA management in school and preschool CCS*

There should be an emphasis on

1. Limiting sharing of food
2. Recognising the risk of changes in routines around eating and sourcing of food.
3. recognising and effectively managing allergic reactions.
4. A “whole school “approach has been shown to be effective resulting reduced reactions and increased societal acceptance of FA within the schools (223). A “whole school” approach, is where policies are developed in partnership with parents, pupils and healthcare professionals and involve “whole school” education—pupils, teaching and non-teaching staff alike (206).

Conclusion

Irish children are having allergic reactions in preschool CCS and school. This mirrors closely the international experience. Schools are using ineffective prevention models such as “nut bans” and failing to recognise that prevention of food sharing is more effective. The emergency response to anaphylaxis in Irish schools is poor. The provision of education within the tertiary allergy clinic setting cannot prevent these incidents from taking place but ensuring AAP are provided by parents to each school and preschool is a role for the clinic team . Prevention beyond that will require structured policies, with government involvement.

Chapter 5: An educational tool for parents of children with newly diagnosed nut allergy: a randomised control trial

SECTION 5.1: INTRODUCTION

The preceding chapters have provided the reader with an insight into many aspects of the lives of food allergic children in Ireland. These children are living with allergy, taking part in social activities, visiting food establishments, and appropriately attending preschool CCS and school. Allergic reactions are occurring but most, fortunately are mild and happen at home in the presence of their parents. This chapter reports on an interventional study, examining the effect of learning the outcomes of ReAACT on QoL and anxiety of parents of newly diagnosed food allergic children

Quality of life and anxiety in food allergy

The main risk with FA is that of AARs, specifically a severe reaction and risk of death. Although this risk is very low (238), it is perceived as much higher by parents, which causes anxiety and impacts on their QoL (246-248). In particular, the initial diagnosis of FA is often a very anxious time and parents report feeling overwhelmed both by the diagnosis and by the amount of information they have to digest (249). Therefore, it is not surprising that parents of younger children with FA report poorer QoL compared to parents with older children with FA (250). Unfortunately, this need for psychosocial support is largely unmet due to lack of psychologists equipped to work with FA families especially in Ireland. Furthermore, effectiveness of psychosocial interventions in FA has been under-addressed and was recently assigned as one of 4 research priority areas (251).

Learning to cope with FA and potential drivers of poor QoL and anxiety

A parent's ability to cope with their child's FA is a dynamic process which can fluctuate over a child's developmental life and FA journey and as such we can hypothesise that QoL will also fluctuate (252). This may be one of the reasons why QoL is variable across studies. The time of initial diagnosis of a nut allergy is a critical time (253). This period extends from the original reaction to the first allergy appointment when the diagnosis is confirmed. Both at diagnosis and indeed throughout the childhood, there are a number of factors which can increase anxiety. Mandell et al interviewed 17 families regarding their life with FA; they describes fluctuations between periods of normalcy and periods of crisis as a dominant theme (77). Anxiety levels tend to be very high at diagnosis which in turn motivates information gathering and vigilance but then dissipates over time as parents adjust to living with FA (8). Children are heavily influenced by their parents coping strategies with their medical condition and will adopt these as they get older and approach adolescence (254). Certain events that can retrigger anxiety levels e.g. an accidental

reaction and change in a child's developmental stage (77). He highlights middle childhood (6-11years) as being a particularly difficult time for parents. This is when children better understand their own allergy, however, may not be able to adequately protect themselves. In ReAACT, we have seen that this group are more restricted in their eating out behaviours when compared to younger or older food allergic children (Table 2.4, section 2.3 , chapter 2).

Indeed, an association between news media consumption and parents' and children's fear of fatal allergic reactions to food has been reported (255). The psychological theories of availability heuristic (people make judgements on the likelihood of an event on how easily a case comes to mind) (256) and base case neglect (erroneously judge the likelihood of a situation by failing to consider all relevant data, instead, focusing on new information) (257) can help explain how heavy reporting of rare severe/fatal AAR cases in the media can increase anxiety among food allergic parents and children leading to avoidance of certain activities.

Even in peer reviewed literature, there appears to be a focus on reporting negative findings with respect to QoL, a multitude of papers on the topic. We do not want to underestimate the burden of FA, however the bombardment of FA parents with negative FA stories is unhelpful. We do know that a small level of anxiety can be helpful at ensuring vigilance and avoiding risk taking behaviour (7). However, when it becomes excessive and parents wish their food allergic child to avoid situations in which the risk of accidental ingestion is very low, they can feel a temporary relief that inadvertently drives increased anxiety via a spiral of negative reinforcement (111).

Improving QoL and anxiety

One of the goals of our allergy clinic is the provision of evidenced based accurate information to parents, particularly at diagnosis. We aim to normalise FA for families, without minimising the risks associated with it. A recent study from our own department demonstrated that a handout, dispelling commonly held myths around FA , significantly improved the QoL of parents awaiting an allergy appointment and reduced their FA related anxiety (PAAM 2021 abstract No44). (It was our goal to design an additional, effective education tool that would improve parental QoL subsequent to their child's FA diagnosis).

We do know that previous qualitative data has reported parents wishing to communicate with other parents of children with FA (258). Vargas et al found that parents of FA children see other parents as a useful resource of information particularly at diagnosis. Mandell found that adequate information, both medical and non-medical, a supportive environment and an awareness of how other parents managed, helped parents of food allergic children feel supported at diagnosis . In

this study, we are interested in finding out whether awareness of the successful management, by a greater number of families with nut allergy in Ireland, would impact on level of anxiety and health related QoL of those newly diagnosed with nut allergy?

Design of a psycho-educational intervention tool using the results of ReAACT

It was identified in the previous chapters that the vast majority of the food allergic children in ReAACT are participating in age-appropriate social activities and visiting eateries and are thereby “living with allergy” (chapter 2).

We hypothesized that providing the parents of newly diagnosed children with FA with information on how social inclusion and low levels of allergic reactions is the norm amongst older Irish food allergic children, would have a positive impact on their QOL and level of anxiety and promote “living with risk” rather than “living with fear”.

We have used the results of ReAACT to design a psycho-educational intervention tool (discussed further in section 5.3). Specifically, in this part of the study, we aim to assess the effectiveness of this specially designed psycho-educational intervention (illustrating the routine practices of food allergic children regarding social activities and eating out and their reaction rate- results of chapters 2-4) on disease-specific QOL and level of anxiety of newly diagnosed parents and children.

Our research question: Is a psycho-educational intervention (illustrating the routine practices of food allergic children regarding social activities and eating out) compared to no intervention, effective at improving disease-specific quality of life and reducing level of anxiety of newly diagnosed parents and children (age 6 to 36 months) with nut allergy in Ireland?

Objectives:

1. To identify and recruit nut allergic children for this study.
2. To collect relevant background data
3. To randomise participants into two groups (control and intervention). Intervention group will receive the educational tool booklet. The control group will not.
4. To administer four validated questionnaires at the start of the study and 2 weeks after the participants have received the educational tool.

Main Outcome:

Change in scores of following questionnaires following intervention (psycho-educational tool) or no intervention:

1. Food Allergy Quality of Life Questionnaires (FAQLQ parental proxy form)
2. Food allergy quality of life parental burden form (FAQOL PB)
3. State and trait anxiety inventory (STAI)
4. Self-efficacy in Food Allergy Questionnaire (SEFAQ) Parent Proxy.

SECTION 5.2: LITERATURE REVIEW

There is an abundance of literature on QoL and emotional wellbeing in both parents and children with FA. This literature review focuses on parents and caregivers, looking at the evidence pertaining to their QoL. The review covers studies reporting on interventions that have been shown to improve QoL of parents with FA children. It also examines educational theories relevant in the design of an educational tool for parents and lastly, looks at any evidence that exists to help in the design of such an educational tool.

QoL and anxiety in parents of food allergic children

Recently, there has been more attention given to managing the psychosocial issues associated with FA such as poor QoL and anxiety (259). Consequently, there is an abundance of literature in this area; There appears to be a large variation in QOL among parents of children with FA (67) with a number of studies reporting a decreased disease specific QOL in parents (260, 261).

Peanut allergy in particular, appears to have a serious impact on the caregivers QOL (with high levels of anxiety in both mothers and father (262). The mother seems to be disproportionately affected (260). Differences in involvement in the care of their food allergic child rather than other gender differences may explain discrepancies in mothers and fathers perceived impact on their QoL (263). Parents also appear to be affected more than the allergic child. Knibb found that parents of food allergic children had poorer QOL compared to parents with non-allergic children but that allergic children had similar or higher QOL than non-allergic children (264).

There are a number of reasons why parents of FA children have a lower QOL and/or higher anxiety levels. The potential impact FA has on social activities and eating out habits may be one of the contributors of decreased QOL (265). Difficulties finding food without allergens, time required for label reading (62) and the daily possibility of AARs and anaphylaxis in their child are other contributors; Indeed, 70% of parents spend > 5 minutes checking labels. Interestingly, poor QOL appears to be significantly more likely among caregivers who are more knowledgeable about FA as well as those who have children with multiple FA (67).

Sourcing information on food allergy by parents

Parents seek FA information from non-medical sources such as the Internet and support groups. Over 77% of Irish adults use the internet daily and one study finding that 67% of parents of food allergic children using social media (266).

Ireland, in particular has a persistently high demand for web-based information relating to allergy as evidenced by comparing google trends for allergy searches in Ireland in 2015 and again in 2019 (267). However, the proportion of evidence-based websites encountered by the Irish public is considerably lower than that encountered by patients in other urban centres. This is of concern particularly as access to allergy services in Ireland is limited, so online information of varying quality may be relied upon by parents. Inaccurate information could result in increased anxiety. Parents may also not be able to distinguish between reliable and inaccurate sources. Çelik et al found that 64% of parents of food allergic children reported that the information obtained on the internet and the information provided by the physicians was contradictory (268). YouTube videos on FA frequently recommend controversial diagnostics and commonly depict non-IgE-mediated reactions (269). Jones et al found a large number of resources online for FA related to emotional wellbeing; however these were of variable quality and many lacked evidence base (270).

The internet is also a place of information exchange between parents with almost half of parents in Celik's study reporting they regularly give FA advice to other parents online (268). Vargas found that parents of newly diagnosed children see other parents as a useful resource of information particularly at diagnosis (249). A survey of a FA online support group found the benefits to be accessibility, receipt of social support as well as guidance on coping strategies (271).

But does accessing all of this information translate into improved QoL outcomes? Ditzler et al found high trust in online information sources was negatively associated with QoL (272). They also found that advocacy group membership had an independent negative association with QoL. This might reflect the unregulated information that they might receive from online support groups and blogs through these groups.

Interventions to improve QoL

There are a number of validated QoL questionnaires (273, 274) that are widely used in the literature which allows comparison of different interventions. However, there is a paucity of studies that look at interventions that improve QoL in caregivers. Existing interventions for parents

shown to improve QoL include cognitive behavioural therapy (275), a self-regulation intervention (276), or a once off group intervention (277).

In a recent systematic review of interventions that targeted well-being and support for caregivers of children with FA, the authors concluded that cognitive-behavioural strategies may benefit some mothers, but that few studies of these interventions were methodologically sound (278). Brockow et al describe a structured educational intervention delivered in a group setting by 2 sessions of 3 hours (modelled on previous successful programmes in asthma and eczema) for caregivers of children at risk of anaphylaxis (279). It was delivered by a multidisciplinary team of allergists, psychologists, and dietitians. They showed a significant decrease in caregiver anxiety (as measured by the Hospital anxiety and depression scale) in their sample of 95 caregivers. They did measure QoL and provided minimal details of the content they covered (recognition of anaphylaxis, daily strategies such as label reading and food preparation, risk reduction measures, coping with anxiety and administration of an epinephrine auto-injector).

The involvement of other parents in education at diagnosis has been shown to be valued by parents of newly diagnosed children (280) and experienced parents with FA have reported that parents of newly diagnosed FA children would benefit from clear information at diagnosis (249). An online social network designed as peer support for families of children with FA was not found to result a change in FAQL but was acceptable to parents (281).

Educational theories for learning.

Any review of the literature on educational interventions would not be complete without a brief examination of the relevant educational and learning theories. The educational theories of constructivism and cognitive theory of learning are important to discuss. The theory of constructivism states that, learner's construct understanding or meaning by making sense of their experiences and fitting their own ideas into reality (282). Constructivism says that students come to learning situations with a variety of knowledge, feelings, and skills, and this is where learning should begin. Their existing knowledge and beliefs on a topic are their "schema". An educational programme tool should aim to understand the learner's (parent's) knowledge base and intentions and present information, so it fits into the learner's (parent's) schema (283). The literature reviews in chapters 2-4 have helped us to identify potential drivers of anxiety and poor QoL above, this has allowed us to choose specific types of information to give to parents.

The social cognitive theory of self-efficacy is also relevant here. Confidence and 'the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations' has been defined as self-efficacy (284). Multiple factors influence self-efficacy. In

particular, social persuasion and experiences (modelling by others) as well as past experiences all influence one's self-efficacy judgement and impact on behaviour (284). Knibb et al showed that self-efficacy is the best predictor of quality of life in parents with FA children as evidenced by the FAQL-PB (285). Increased self-empowerment (a related concept), has also been found to be associated with increased QoL (286).

Designing an educational tool

Prior to designing an educational tool for parents, it is important to review the literature on the characteristics of an effective tool. Chapman highlights that careful consideration of not only the material to be presented but also of the visual format by which it is presented is critical for any successful learning experience (287).

A number of challenges are reported in designing material for patients. Readability and usability problems with patient information sources appear to be ongoing problems (288). Payne et al found that large numbers of target audiences may be unlikely able to comprehend important aspects of information sources because of their content, writing style or organisation (289). Infographics and images help to provide information graphically which is more likely to be remembered than text (290). The use of colour in resources is also important to reflect upon. The mere use of colour can influence a person's judgement towards a particular choice (291). Colour has the potential to enhance communication, but design mistakes can result in colour figures that are less effective than grayscale displays (292).

The medium that text is read within, plays an influential role for certain readers (293). There are a number of studies which examine reading comprehension in the digital age, and all find that paper is better than screen (293-295). Singer et al suggested that readers read too quickly from a screen (293). Reading on a screen is potentially more interactive with digital add-ons (interactive quizzes, pop out features). However, there isn't yet convincing evidence that digital add-ons improve reading comprehension or even match the reading comprehension that can be achieved with text on paper and well-designed studies are needed.

Conclusion

Parents of food allergic children are at increased risk of decreased QoL as well as anxiety. This is especially true for (i) parents of younger children and (ii) at diagnosis of the FA. Many of the studies on QoL in caregivers are those of nut allergic children. We know that parents value information

from other parents and often use the internet to access this information. Unregulated information can lead to poorer QoL. There is a paucity of literature on interventions or tools that specifically aim to improve QoL in parents of food allergic children. Any that do exist are labour intensive and are not straight forward to implement. With the increased recognition of the psychosocial pathology in FA, a need for easy-to-use tools which are effective and produce meaningful outcomes for parents are urgently required.

SECTION 5.3: METHODS

Participants and study design

A prospective controlled trial intervention study was carried out in the Allergy department in Children's Health Ireland (CHI) at Crumlin. The participants were parents of children between 6 and 36 months with a new diagnosis of a nut allergy. As this diagnosis was new, it ensured parents had not had time to develop strategies relating to social activities and eating out.

The following were the inclusion and exclusion criteria:

Inclusion criteria:

1. Children between 6 months and 36 months.
2. Newly diagnosed nut allergy defined as a clinical reaction with a skin prick test (SPT) of $>3\text{mm}$ or sensitised with SPT $>7\text{mm}$.
3. Parents of children were 18 years and over.

We chose to include parents of nut allergic children; it is widely reported that having a nut allergic child can increase anxiety and decrease QoL (260, 296). There is not the same body of data available for QoL in parent of young children with cow's milk or hen's egg allergy.

Many of these children were prescribed AAls as per international guidance (117).

Exclusion criteria:

1. Siblings of food allergic children, as these parents would already have well established coping strategies.
2. Participation in another research study.
3. Chronic conditions that might cause anxieties in social environments and impact activities of daily living e.g. diabetes, cystic fibrosis, autism, epilepsy.
4. Parents of ex-premature infants- due to known anxiety and maladaptive coping strategies.

Recruitment

Parents were contacted by phone if they had attended an allergy outpatient appointment in the last 6 months. The study was explained to the parents over the phone. Once a parent had agreed to participate, they were sent a link via text message from the CHI allergy department research mobile phone.

Procedure

Participants clicked on the link sent via text message. This brought them to the online database Qualtrics and to a copy of the study patient information leaflet (PIL) . They then completed the online consent form and were thus enrolled in the study. After enrolment, participants were prompted to make their own study identification number using the day and month of their birthday and the initial of their surname. All data collected was linked to this study ID number which ensured anonymity. Participants were then brought to the study questions within Qualtrics and completed the following 5 questionnaires online at baseline (see appendix for copy of questionnaires).

Measures

1. Food Allergy Quality of Life Questionnaire (FAQLQ).
The Food Allergy Quality of Life Questionnaires (FAQLQ) are disease-specific developmentally appropriate measures that have been developed to assess health related quality of life (HRQL) in FA for all age groups and parents and are the most frequently used HRQL tools in FA research and practice. These include the Parental Burden (PB) , Parent Proxy Form (PF) (274), the Child-form (CF), the Teen form (TF) and the Adult form (AF). The questionnaires can be used to measure cross-sectional differences in quality of life between patients at a point in time - or longitudinal changes in HRQL. Research has shown that the measures are valid, reliable and are responsive to important clinical changes (274, 297, 298). In this study we used the FAQLQ parental proxy form (PF) (Appendix Y).
2. The Food Allergy Quality of Life—Parental Burden Scale (FAQL-PB)

Food Allergy Quality of Life Parental Burden (FAQL-PB) was developed and introduced in 2004 by Cohen et al (273) as a specific questionnaire to measure the burden of food-allergic patients on caregivers and was utilized in several further studies (71, 299). The FAQL-PB is a 17-item scale that uses a 7-point Likert scale ranging from 1 (not troubled) to 7 (extremely troubled). Items concern issues such as going on vacation, social activities, worries, and anxieties over the previous week. A higher total score is indicative of greater burden on the parents. The scale has excellent internal consistency.

3. State Trait anxiety Inventory (STAI)

The State-Trait Anxiety Inventory (STAI) is one of the most used self-report measures of anxiety in research and clinical settings across different cultures. This instrument was developed by Spielberger, Gorsuch, and Lushene (1970). State anxiety refers to a transitory emotional state characterized by subjective feelings or tension that may vary in intensity over time. Trait anxiety refers to a relatively stable disposition to respond to stress with anxiety and a tendency to perceive a wider range of situations as threatening. The STAI is composed of two different scales: one related to state anxiety (STAI-S) and one related to trait anxiety (STAI-T). The STAI-S scale has 20 items that are answered on a 4-point Likert scale based on “how you feel right now, at this moment.” The STAI-T scale also has 20 items that are answered on a different 4-point Likert scale based on “how do you generally feel” (Appendix Y).

4. Food Allergy Self-Efficacy Questionnaire (FASEQ) Parent Proxy form

This has been shown to be a valid tool in assessing caregiver FA self-efficacy. Self-efficacy is a distinct but related concept that captures aspects of self-management that are an important companion to health-related quality of life (300).

5. Food Allergy Independent Measure (FAIM)

The Food Allergy Independent Measure (FAIM) is an independent measure of QoL with which FAQLQ scores can be correlated. It was developed to measure construct validity in the FAQLQs and it is valid relevant and reliable (301). It has 6 questions which captures participants expectation of outcome. It is widely used in the literature in ensuring construct validity within QoL studies in FA.

Randomisation

At enrolment, participants were randomised into group 1 (intervention) or group 2 (control). Simple randomisation using online random number generator was utilised.

Group 1 (intervention group) were sent the psycho-educational intervention (booklet) after completion of the baseline questionnaires. Both Group 1 (intervention group) and Group 2 (control group) received routine care in the allergy clinic, consisting of education (avoidance and management of AARs and when and how to use adrenaline) given by the allergy team. This allergy education is described in detail in chapter 1 (Section 1.1). Two weeks after the educational booklet was sent out to Group 1, both groups were requested to complete the 5 online questionnaires for a second time. A different link was sent to Group 1 and Group 2 to distinguish participants. Two reminders were sent to each group a week apart to complete the questionnaire. Data collection ended 2 weeks after the 2nd link to the questionnaires was sent out. On completion of the questionnaires, the data was transferred immediately to the online data reservoir in Qualtrics which was only accessible by the study team.

Intervention

The psycho-educational tool was delivered as a booklet (Appendix Y). It was designed using the results from the first 6 months of data collection in ReAACT as described in Chapters 1-4. Content focused on the day-to-day social activities of children with FA. It is composed of text with colourful graphics. The content was designed by 3 researchers, all working in the field of paediatric allergy. Each double-page provided information on a specific topic such as eating out, parties, visiting friend's houses, Christmas time etc. Quotes from parents in ReAACT were provided for each topic, this gave the parent's a voice.

e.g. Topic 1: Attending birthday parties. The pages provided information on the number of children with FA attending parties and number of AARs that occur there. There are quotes from 2 parents describing their experience at parties with their food allergic child. Each section finishes with a "take home message" at the end of the page (figure 5. 1).

Figure 5.3.1: Sample of a page from the educational tool

I want my child to go to birthday parties, just like other kids.
Is that going to be unsafe for them to do?

Here's what we found out:

Almost all (94%) of our study group, aged 5 to 12yrs, attended birthday parties.

Almost half brought their own food to the party.

Only 5 reported an allergic reaction. None were severe.

What parents say

Maire: "I always speak with the parent beforehand. The majority are very obliging".

Lorna: "Parents are so much more aware now. It makes parties so much easier for my now 11yr old."

Take home message:
With a little planning, food allergic children can have fun and stay safe at these important events.

The study was approved by the Children's Health Ireland, Research Ethics Committee.

Sample size calculation

Our calculation was based on two independent groups, with a continuous endpoint, a minimal clinically important difference of 0.5 for FAQLQ +/-1, Alpha 0.05, Beta 0.2 Power 0.8.

$N (88 + 12 \text{ drop out}) = 100$ ratio 1

$k = n_2 n_1 = 1 n_1 = (\sigma_1^2 + \sigma_2^2 / K) (z_{1-\alpha/2} + z_{1-\beta})^2 \Delta^2 n_1 = (12 + 12/1) (1.96 + 0.84)^2 0.62 n_1 = 44 n_2 = K * n_1 = 44 k =$

$n_2 n_1 = 1 n_1 = (\sigma_1^2 + \sigma_2^2 / K) (z_{1-\alpha/2} + z_{1-\beta})^2 \Delta^2 n_1 = (12 + 12/1) (1.96 + 0.84)^2 0.62 n_1 = 44 n_2 = K * n_1 = 44$

$\Delta = |\mu_2 - \mu_1|$ = absolute difference between two means

σ_1, σ_2 = variance of mean #1 and #2

n_1 = sample size for group #1

n_2 = sample size for group #2

α = probability of type I error

β = probability of type II error

z = critical Z value k = ratio of sample size for group #2 to group #1

Therefore sample size for group 1 (intervention) is 44 and for the control group is 44.

Data processing and analysis

Descriptive statistics

Descriptive statistics was used to analyse demographic and clinical characteristics. The data was tested for normality (Kolmogorov-Smirnov, Trimmed Means, and QQ Plots) and assumptions for inferential analyses were found to be met. Data was summarised by treatment group. In summary tables of continuous variables, the minimum and maximum statistics, the arithmetic mean and median, the 95% confidence interval and standard deviation (SD) were presented. In summary tables of categorical variables, counts and percentages were used.

Construct Validity and Discriminative Validity of the FAQLQ-PF and FAQL-PB

Pearson's correlation coefficient was used to examine relationships between measures (the questionnaires listed above). We expected a significant correlation between FAIM and FAQLQ-PF and FAQL-PB, and between FAQLQ-PF, FAQL-PB and FASEQ. We also expected a significant relationship between S-Anxiety and FAQLQ-PF, FAQL-PB and FAIM. To test the discriminative validity of FAQLQ-PF and FAQL-PB, we used an analysis of variance (ANOVA) to examine if there was a significant difference according to number of reported allergies (0-3 vs 4+), and the number of foods avoided (0-3 vs 4+).

Impact of the ReAACT intervention

Paired sample t-tests (split by intervention and Control) were done to examine if there was a significant difference in scores on the questionnaires pre/post intervention for either group. Following this, we used an ANCOVA to examine if any difference found held, when controlling for number of reported food allergies.

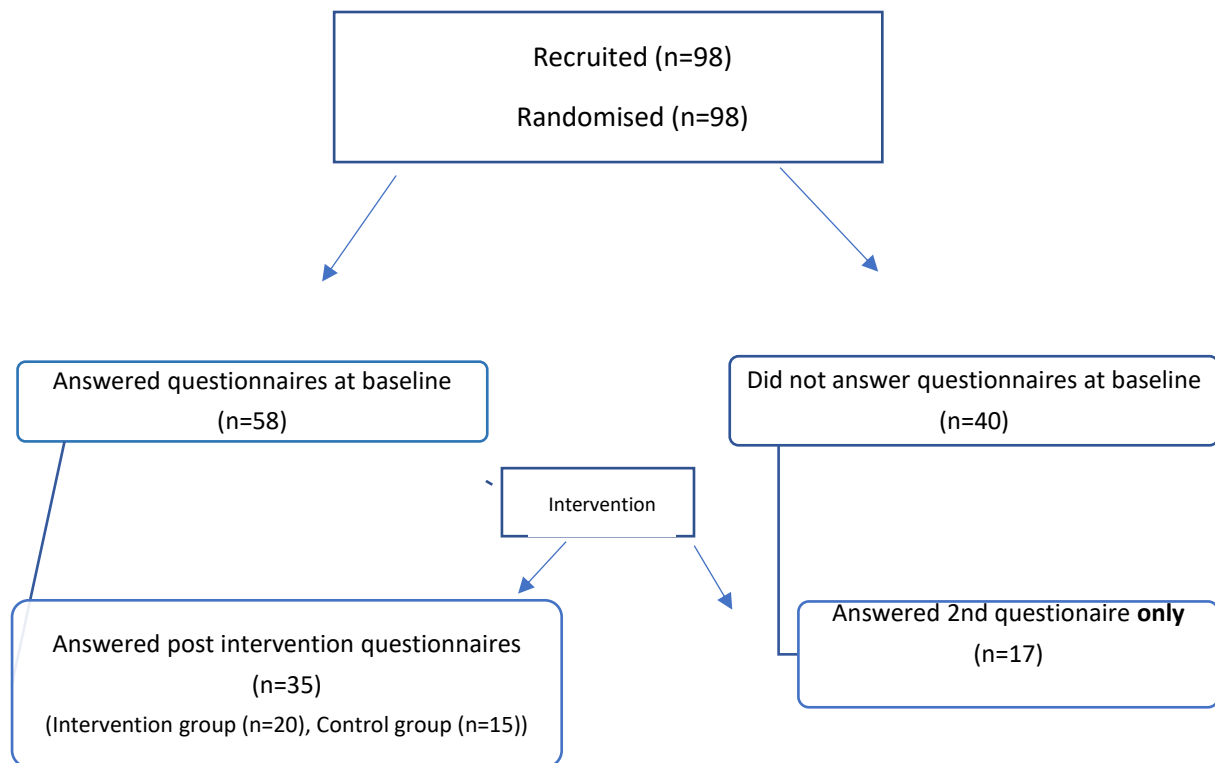
All analyses were performed in SPSS for Windows version 27 (SPSS Inc., Chicago, IL). Changes were regarded as statistically significant if the two-tailed p value is < 0.05 .

Section 5.4: RESULTS

Participants

98 were invited and consented to participate in the study. Fifty-eight participants (59%) answered the questionnaires at baseline; 35 (60%) of these completed the post intervention questionnaires; 20 in the intervention group and 15 in the control group. Figure 5.4.1 illustrates the flow of participants through the study.

Figure 5.4.1: Flow of participants through the study



Results of the independent sample t-tests indicated that there were no significant differences in baseline scores on any measure between those who completed the questionnaires at baseline (n=58) and those who took part in the intervention study by completing the questionnaires again (n=35) : FAQLQ ($t(56) = -0.468, p = 0.641$), FAIM ($t(56)=0.167, p=0.868$); SE ($t(56)=-0.577, p=0.567$); PB ($t(56)= 0.444, p=0.659$). Therefore, we can assume that the participants were equivalent in profile, and that factors other than those directly related to the study were responsible for 'drop-outs'.

Furthermore, no significant differences were found between those who completed the baseline questionnaire and those who took part in the study according to when they were diagnosed ($t(54) = -01.811, p = 0.076$), who they were diagnosed by ($t(54)= -.324, p=0.747$) or 'how normal their child's life is compared to children without FA ($t(54)= .265, p=0.792$).

Profile of participants

Clinical and demographic data was collected for 76 participants.

The median age of participants was 22 months (LQ, UQ). 83% of children were born in Ireland.

The median age of parents was 37 years (LQ, UQ). 79% were prescribed adrenaline autoinjectors. (Table 5.4.1)

Table 5.4.1: Demographic and clinical details of participants

| | All participants (n=76) | Participants completed baseline questionnaire (N=58) | Group 1 (intervention) (N=20) | Group 2 (control) (N=15) | P value |
|---|-------------------------|--|-------------------------------|--------------------------|---------|
| Age of child (months) Median (LQ, UQ) (months) | 22(19-23) | 22 (18-23) | 21.5 (17-23) | 22.5 (17-24) | |
| Country of birth n(%) | | | | | |
| Ireland | 63 (83%) | 49 (84.5) | 17 | 11 | |
| United Kingdom | 14 (17%) | 9 (15.5) | 1 | 6 | |
| Other | | | 2 | 0 | |
| Age of parent (years) Median (LQ, UQ) | 37 (33-39) | 37 (33-39) | 37 (34-39) | 36 (33-38) | |
| Gender of parent n(%) | | | | | |
| Male | 8 (10.6) | 5 (17) | 2 (10) | 3 (20) | |
| Female | 68 (89.4) | 53 (83) | 18 (90) | 14 (80) | |
| Number of food allergies n(%) | | | | | |
| 1-3 | 67 (88) | 50 (86) | 17 (85) | 13 (87) | |
| ≥4 | 9 (12) | 8 (14) | 3 (15) | 2 (13) | |
| Food allergy | | | | | |
| Cow's milk | 25 (33) | 20 (34) | 6 (30) | 5 (33) | |
| Hens egg | 41 (54) | 33 (56) | 11 (55) | 8 (53) | |
| Peanut | 56 (75) | 40 (69) | 13 (65) | 12 (80) | |
| Treenut | 58 (76) | 36 (62) | 11 (55) | 11 (73) | |
| Other (legumes, sesame) | 4 (7) | 3 (5) | 1 (5) | 4 (27) | |
| Adrenaline autoinjectors prescribed n(%) | 60 (79) | 49 (84) | 16 (80) | 14 (93) | .264 |

Construct Validity of the Measures

We used the Pearson's correlation coefficient to examine relationships between all measures. As expected, we found significant correlations between FAIM and FAQLQ-PF and -PB, and between FAQLQ-PF, -PB and SE. We also expected and found a significant relationship between S-Anxiety (but not T-Anxiety) and FAQLQ-PF, -PB and FAIM.

Table 5.4. 2: Pearson’s correlation coefficient demonstrating the relationships between (a) FAQLQ and FAIM, (c) SE and state and trait anxiety inventory and (c) state and trait anxiety inventory and FAQLQ

(a)

| | FAQLQ Baseline | FAQLQ Post | FAIM Baseline | FAIM post |
|----------------|----------------|------------|---------------|--------------------|
| FAQLQ baseline | 1 | 0.653 *** | 0.451 *** | 0.357 * (0.018) |
| FAQLQ post | 0.653 | 1 | 0.295 | 0.625 |
| FAIM baseline | 0.451*** | 0.295 | 1 | 0.573 |
| FAIM post | 0.18 | 0.625 | 0.573 | 1 |

*p<.05
 ** p<.01
 *** p<.001
 Abbreviations: FAQLQ: food allergy quality of life questionnaire; FAIM: food allergy independent measure. Post: post intervention.

(b)

| | SE baseline | SE post | FAIM baseline | FAIM post |
|---------------|-------------|---------|---------------|-----------|
| SE baseline | 1 | 0.555** | 0.397* | 0.424* |
| SE post | 0.555** | 1 | 0.392* | 0.471** |
| FAIM baseline | 0.397* | 0.392* | 1 | 0.591** |
| FAIM post | 0.424* | 0.471** | 0.591** | 1 |

*p<.05
 ** p<.01
 *** p<.001
 Abbreviations: FAIM: food allergy independent measure. Post: post intervention; SE: self-efficacy.

(c)

| | Trait post | State post | FAQLQ post |
|------------|------------|------------|------------|
| Trait post | 1 | 0.710*** | 0.134 |
| State post | 0.710*** | 1 | 0.326*** |
| FAQLQ post | 0.134 | 0.326** | 1 |

*p<.05
 ** p<.01
 *** p<.001
 Abbreviations: FAQLQ: food allergy quality of life questionnaire;
 Post: post intervention.

There was a significant difference in the number of reported allergies according to FAQLQ-PF ($F(1, 34) = 5.19, p = 0.029, \text{partial } \eta^2 = .136$) and the FAQLQ-PB ($F(1, 34) = 5.65, p = 0.023, \text{partial } \eta^2 = .136$), with higher mean FAQL impact for those with more reported allergies. We also found a significant difference according to the number of foods avoided for both the FAQLQ-PF ($F(1, 49) = 5.624, p = 0.022, \text{partial } \eta^2 = .105$), and FAQLQ-PB ($F(1, 49) = 5.470, p = 0.024, \text{partial } \eta^2 = .102$), with a higher mean FAQL impact for those who avoided more foods.

Impact of the educational tool intervention

(i) Improvement in quality of life

There was a significant improvement in QOL for those in the intervention group as compared to the control group. This is reflected in the significant difference in scores at baseline and following the intervention in the intervention group only for FAQLQ- PF ($t(19) = 3.111, p = 0.006$) and for the FAQL- PB ($t(19) = 3.285, p = 0.004$) but not for the control group for FAQLQ- PF ($t(14) = 1.962, p = 0.070$) or for FAQL- PB ($t(14) = 1.327, p = 0.206$). There is also a larger mean difference in scores between experimental (0.47) vs control groups (-0.336) for baseline and post intervention scores for the FAQLQ- PF. The same was true for the FAQL -PB for intervention group (0.826) but not in the control group (0.245).

(ii) Improvement in anxiety scores

There was a significant difference in state anxiety scores at screening and following the intervention for the experimental group ($t(19) = 3.328, p = 0.004$) but not for control group ($t(14) = 0.482, p = 0.637$). Trait anxiety scores were also improved (not significantly) in the intervention group ($t(19) = 2.53, p = 0.020$) but not in the control group ($t(14) = -0.604, p = 0.555$).

There was also a larger mean difference in the state anxiety scores between intervention (8.65) and control groups (1.86) for baseline and post intervention scores.

(iii) Improvement in self-efficacy

There was an improvement in parent's self-efficacy scores between baseline and post intervention for the experimental group ($t(19) = 2.057, p = 0.050$) but not for the control group ($t(14) = 0.118, p = 0.908$). There was also a larger mean difference in self-efficacy scores between intervention (0.47) vs control group (-0.336) for baseline and post intervention scores.

SECTION 5.5 DISCUSSION

We have shown that an educational intervention delivered in a booklet format to parents of newly diagnosed, infants and toddlers with nut allergy, resulted in a significant improvement in disease specific QoL, parental anxiety levels and self-efficacy. The intervention illustrated the routine practices of Irish food allergic children with regards to social activities and eating out as well as well as displaying some evidence of reaction rates.

The improved QoL is reflected in the significant difference in scores at baseline and following the intervention in the intervention group only for both questionnaires, FAQLQ- PF ($t(19) = 3.111$, $p = 0.006$) and for the FAQL- PB ($t(19) = 3.285$, $p = 0.004$). Previous literature reports a higher FAQL PB (greater burden) score if the child was allergic to >2 foods ($P < 0.0001$) (302). We went a step further and showed that the educational intervention resulted in a higher mean FAQL impact for those with more reported allergies and more food avoidances.

Parental anxiety levels were also significantly improved after viewing the educational tool. There was a significant difference in state anxiety scores at screening and following the intervention for the experimental group ($t(19) = 3.328$, $p = 0.004$) but not for control group ($t(14) = 0.482$, $p = 0.637$). Feng makes the point that the stress from having a FA may be more burdensome than the FA itself (303). It is possible that the information provided in the educational tool has resulted in a shift in participants thoughts around FA, which in turn impacts on their feelings (decreased anxiety) which has in improved QoL and potentially changed behaviours. Both parent and child are likely to benefit from this decreased anxiety. Le Bovidge et al demonstrated that psychological distress in children with FA was significantly associated with maternal anxiety, and these authors suggested that treatment of parental anxiety would improve outcomes for children with FA (304).

Self-efficacy was also improved in the intervention group. Previous work has shown that parents with lower FA self-efficacy, have poorer psychological outcomes, (higher anxiety and post-traumatic stress) (248). Knibb et al also showed that self-efficacy is the best predictor of QoL in parents with food allergic children as evidence by the FAQL-PB (250). Therefore an intervention such as ours, that is effective at improving self-efficacy in these parents, is to be welcomed. Although no intervention have been found to date to be similarly effective for parents with FA children, interventions do exist for adults in other conditions such as asthma which enhance self-efficacy and improve QoL (305).

Previous researchers have looked at group interventions run as workshops and how these might reduce burden associated with FA. One of the first studies to investigate this looked at the benefit of workshops led by a paediatric psychologist on topics such as managing stress and preparing FA children for school showed reduced FA burden by using FAQL-PB and found they were beneficial (277). Another study showed reduced anxiety after attendance at group workshops (279). Neither of these studies were controlled. An individualised self-regulation intervention delivered one to one over a number of phone sessions was effective at improving FA-related QoL for parents of children with FA (using FAQL-PB) (276). This RCT utilised a nurse (a nurse who had previously received a 2-hour training session on self-regulation for chronic disease management).

These interventions all required the use of a person to deliver them (cost and time involved). This contrasts with our tool delivered as a booklet which did not require any extra resources. This is critically important particularly in the Irish setting where there is a paucity of, trained allergists but also, psychologists. The content used in the group interventions discussed above (277, 279), although not described in full in these studies, was standard allergic reaction prevention and management information. The content of our intervention was unique in that it utilised data collected during ReAACT to provide local, relatable evidence of a representative food allergic childhood population partaking in all types of normal social activities. It's content was in stark contrast to the unbalanced anecdotes regarding FA available to parents through social media platforms.

The majority of participants in this study were mothers. The mother is most often the primary caregiver with reported worse FA-related QoL compared to fathers (260). The clinical characteristics of the children of the enrollee parents were also similar across the control and intervention groups. They were all young with an overall median age of 22 months. However, 100% of participants in the control group had been prescribed adrenaline autoinjectors compared to 80% in the intervention group. Prescription of AAI is associated with reduced anxiety for mothers of food allergic children however no significant difference was noted at baseline(71).

The strength of this study is that it uses observational data collected from a clinic population in a unique and novel way to design of an interventional educational tool. This method of education has not been used in previous FA interventions or indeed in other interventions for other chronic paediatric conditions (to the best of the authors knowledge). It could therefore provide a blueprint for future interventions in other chronic conditions.

Another strength of this study is that construct validity was carried out for all measures. A construct in the field of psychology is a skill, attribute, or ability, not directly observable but that

is based on one or more established theories (306) e.g. anxiety, QoL. Construct validity is a type of validity that refers to a test's ability to measure psychological constructs(307). Measures of psychological constructs are validated by testing whether they relate to measures of other constructs as specified by theory (308). In this study, we found significant correlations between FAIM and FAQLQ-PF and -PB, and between FAQLQ-PF, -PB and SE. We also expected and found a significant relationship between State-Anxiety (but not trait-Anxiety) and FAQLQ-PF, -PB and FAIM. These correlations confirm our measures for QoL and anxiety are construct valid.

When studying the effectiveness of an educational tool, it is necessary to choose an outcome that is comparable across studies as well as one that is meaningful to patients (or parents in this case). The 4 measures used here were validated in many populations (as discussed in section 5.3 methods). Reliable and valid measurement tools are a necessary prerequisite to developing and evaluating FA interventions and potential changes in psychosocial impact. A recently published systematic review, identified 13 available parent-report measures assessing the psychosocial impacts of paediatric IgE-mediated FA (309) and highlighted the FAQLQ-PF (used in this study) represented the most widely studied measure to capture outcome to intervention. The FAQLQ-PF also encompasses a meaningful important difference (MID) score to guide interpretation of within-subject change over time, a features that other measures of HRQoL don't have (274). The measures used also ensured that results could be compared within a short interval timeframe---- only needed a 2 week timeframe.

The main limitation identified is that despite the initial response rate of 59% for the baseline questionnaires being in excess of what is expected for an online questionnaire study (25-60%) (310, 311), there was a 40% drop out of participants, between baseline questionnaire and questionnaire post intervention. Participants interests are a prime motivator for responding (312) and this might explain why there was a higher-than-normal original response rate. Parents were keen to see the educational tool. The length of the original questionnaire (20-25 minutes) might subsequently have deterred participants from answering the questionnaire for a second time (post intervention), as has previously been described (313). It is likely that recruitment and response rate in this study were also negatively affected by the malware cyberattack on the Irish Health Service Executive which occurred 3 weeks prior to commencement of data collection. Access to the online questionnaires was sent by a link in a text message. The widely guidance from government/citizens information at the time, was to avoid clicking on any links send by email or text.

We are however, satisfied that there were no differences in between those in the study and those who dropped out. There were no significant differences in baseline scores on any measure between those who completed the questionnaires at baseline (n=58) and those who took part in the intervention study and answered the questionnaires for a second time (n=35, 60%). Therefore, we can assume that the participants were equivalent in profile, and that factors other than those directly related to the study were responsible for 'drop-outs' (n=23).

We have shown that this educational intervention positively supports parents in Ireland who are living and managing nut allergy on a daily basis. By doing so, it provides an innovative contribution to the toolbox that health professionals have in managing families with FA in the absence of skilled psychologists and/or as a complimentary measure. We will continue to follow those in this RCT and assess their disease specific QoL, anxiety and SE at 3 months and 6 months post intervention. Going forward, we plan to provide all parents of newly diagnosed nut allergic children with this educational booklet at the time of diagnosis.

Furthermore, this educational intervention program contributes to our understanding of the impact of this type of information from parents for parents, on the management of FA. It might act as a blueprint for similar educational tools, which could be designed for other atopic conditions such as asthma and eczema.

In summary, these findings are important because they show:

1. This intervention is effective at improving disease specific QoL, state anxiety and self-efficacy.
2. Newly diagnosed parents benefit from information on other parents navigate daily life with their food allergic child (a peer-to-peer model of education).

Chapter 6 Summary of thesis

6.1 Summary

This study provides a unique insight into the life of food allergic in Irish children. This is the first time the burden of FA has been described in the Irish population. Chapter 1 and 2 set the context for the main body of work of the thesis in chapter 3 and 4. The RCT presented in chapter 5 examines a novel educational intervention. This information is vital and provides the Irish allergy community with a great opportunity; It enables improvement of current services and planning of future services; It provides an ability to approach key stakeholders involved with children e.g. schools and the department of education to affect real change.

The data we have collected provides data not been previously reported. It is imperative that we use the positive findings in this study to benefit the wide food allergic paediatric population both in Ireland and beyond.

This final chapter of this thesis will summarise the key findings. I will also discuss 3 important questions by using the findings in our study.

Chapter 1

In chapter one, I provided some background to FA within the context of current Irish society. Until now, the burden of FA has not been defined. I reported the baseline characteristics of the study participants illustrating that they were for the most part similar to those of the general Irish population and to populations attending allergy clinics worldwide. This population with a median age of 7 yrs (LQ 4, UQ 11) were atopic (97% at least one other atopic condition), urbanised (61%), multi-food allergic (66.5%), and of white Irish ethnicity (85%).

Chapter 2

The social activities and the eating out habits of these food allergic children were explored. I report that this population are “living with allergy”; they are participating in age-appropriate social activities and visiting food establishments. A minority are not taking part (8.9% don’t participate in social activities). We aim to identify these children in our clinics by asking about social functioning so appropriate support can be provided. Although 97% of participants visit at least one FE, communication with staff whilst there is poor; only 39% do not inform staff of their child’s FA and 13% do not check all ingredients. Ongoing education in the clinic alongside the introduction of novel methods to enhance and improve parent’s and food allergic children’s with FE staff may teach or augment communication skills.

Chapter 3

In chapter 3, I explored accidental allergic reactions. I set the scene by describing the multiple difficulties in comparing studies on accidental allergic reactions (AARs). IN ReAACT, I found that AARs are frequent in Irish children, their overall annual incidence is 0.44 (95% CI, 0.38-0.50). The majority were mild (86%) and there were no fatalities. The overall incidence (0.54) is significantly higher in younger children (2-4yrs) with milk and egg being the commonly implicated allergens. There was a significantly higher number of severe reactions while on vacation compared to those not on holiday (RR 2.3, 95% CI 1.17-4.58, $p=0.0156$). Almost all reported restaurant related reactions occurred while on holidays. IN over a half of cases the allergen was administered to the child accidentally by the parent. A third of reactions were caused by unidentified allergens which likely reflects a high level of cross contamination. These findings highlight the ongoing need for education on avoidance and management of reactions among food allergic families as well as the wider community.

Chapter 4

In chapter 4, I identified that 12% of the total reactions in school aged children occurred in school, 22% being anaphylaxis. I report that these facilities are poorly prepared to manage FA with only half having a FA policy; One third of these children do not have a copy of their allergy management plan with them in school. Children with an AAP in their school or preschool CSS had a significantly lower risk of an AAR when compared to those without (RR 0.2, 95% CI 0.09-0.47, $P=0.0002$). In clinic we can encourage parents to give a copy of this to the school, however for real prevention beyond that, there will need to be government involvement and policies.

Chapter 5

In chapter 5, I used the data collected in the previous chapters to design an educational tool (booklet format). I assessed its effectiveness in parents of young children who were newly diagnosed with a nut allergy. IN the setting of a RCT with albeit small numbers, I showed the intervention resulted in a significant improvement in disease specific QoL, parental anxiety levels and self-efficacy. These findings need to be replicated in studies with a larger sample size as well as in different populations. However, the design of the tool was novel and it might act as a blueprint in the design of other educational tools for allergic and non-allergic conditions.

I propose 5 questions. I will answer them by using the data described in this thesis.

1. Can accidental reactions be prevented? .

In this study we identified numerous prevention strategies being undertaken. Some of these are based on common sense and consensus (reading labels) and some, such as avoiding all eateries, would generally be discouraged. Evaluating their effectiveness is complicated. It is clear from this study that the association between avoidance measure and prevention is not linear.

For example, in chapter 2, it was recorded that 90% of families visit restaurants on a regular basis. 87% of these reported that they check the ingredient lists if choosing for their allergic child and 65% also inform the waiter of their child's allergy. Backup strategies, in the absence of ingredient lists, included inquiring (61%) making an educated decision (12%) decline ordering (27%). These reported approaches are considered the cornerstones of reaction prevention. Accepting that there will always be variability to people's compliance with prevention strategies (314), with these measures in place, only 1 restaurant-based reaction/12months/entire study group was recorded. However, as reported in chapter 3, once the same cohort went on 1–2-week vacations, 12 similar reactions were recorded. Therefore, the tactics appear to be effective except while vacationing. The factors contributing to the differential effectiveness are undoubtedly multiple and beyond the remit of the studies questionnaire.

What this data offers to our patients immediately is relatable collective experience that they can learn from, if efficiently packaged and communicated. Muraro et al write about the need for structured validated educational programs(259) . The content needs to display the fragility of avoidance measures.

2. Should allergic children in Ireland have disability status in schools?

The pattern of school based, accidental reactions, identified in chapter 4s data could be described as "opportunistic". 78% of reactions took place because an eating opportunity presented itself to a child and they took it! It is difficult to see how most traditional strategies could prevent this type of reaction occurring. Compliance with parental guidance not to eat food, from others is known to be variable in the face of temptation (314). "Nut bans" have been demonstrated to be ineffective internationally (8) and the data from our study reaffirms this. A more complex multipronged approach with effective supervision, capable of real time adaptation to new eating opportunities would need to be considered. Even with this in place, reactions are likely to occur,

including life threatening ones. ReAACT recorded a 100% insufficient response by school staff to anaphylactic reactions. Fortunately, all 4 children recovered however, these cases are cause for reflection. Recent recommendations call for all schools to have stock autoinjectors available (8), but access to adrenaline was not a limiting factor as all had their adrenaline to hand. Effective training is clearly needed but obvious challenges include staff turnover and frequent substitution. In the US, children with a FA are eligible to apply for a 504 Plan which, if successful, will ensure that they are considered a child with a disability, under the law and their school receives accommodations to ensure their academic success and access to the learning environment. The opportunistic nature and the severity of the reactions identified by this large prospective Irish study, coupled with the failure to treat, proposes a need for stakeholders to consider a specific needs category for food allergic children in Ireland.

3. Can allergy health care professionals counteract the negative effect of news media on food allergic parents?

Parents report that they have greatest need for information regarding FA at the time of their child's original diagnosis. Irish people are known to be higher than average users of search engines to source FA related information (267). News reports often present information in a human-interest story format which is effective at evoking interest and emotion. Bute et al have just published evidence that news media stories play a direct role in prompting feelings of fear and anxiety in food-allergic parents (255). Attempts to counter media stories via social media platforms is fraught with risk and not a recommended approach for health care professionals to take (315). The intervention presented in chapter 5 represents a novel method of presenting evidence based, population data in a similarly relatable format as human-interest stories. In contrast, the intervention has been validated using appropriate measures, as a tool for reducing anxiety in parents of newly diagnosed children.

4. "What are the bias and confounding factors in ReAACT?"

This piece of work does have some limitations in the form of bias and confounding factors that have already been touched on in the relevant chapters.

We did not include children with uncontrolled eczema as it can be difficult to distinguish IgE mediated AARs from flared eczematous skin. However, only one child was excluded for this reason.

Ethnic minorities were not actively sought out. This study population aimed to be representative of the population attending an allergy clinic and was not specifically looking at allergic reactions in these minority groups. It would be useful to design a further study to actively seek these children and understand if they were attending clinic, did they understand education and were they ultimately more at risk of AARs.

There was a higher number of urban dwellers in this study due to the catchment area of the service. This is a bias, as rural areas are more at risk when reactions occur due to decreased accessibility to services and increased levels of deprivation (31, 36).

If a child swapped groups, the group that they were in at the end of data collection, was the group within which they were analysed. We did not want a child to be in more than 1 group during the study. This is a potential bias but is difficult to avoid. A future study might leave participants in the age group they were placed at recruitment; however, this would also introduce bias.

There were five episodes of participants contact during the study. In 98% of cases, the same parents was spoken to at all five episodes. In 85% of cases, this was the mother. This was unintentional and is a potential bias; however, in each case either the child attended with their mother, or her contact details were listed as first next of Kin. In much of Irish society, the mother retains the role of primary caregiver irrespective of her employment status and therefore data collection from her likely enhanced data correctness. Highlighting these confounders may help with guide future research in this area.

5. “What are the Future Directions for the Irish Children with Allergic Disease?”

The data reported here provides a huge opportunity to positively influence the lives of food allergic Irish children. This study provides local information; collected from a cohort of children whose experiences are representative of FA allergic children nationwide in this small country. To optimise their participation in normal social activities, early identification of food allergic children with restrictive patterns of socialisation as part of a routine clinical review is essential. Adolescents are an at risk groups in terms of social and eating out restrictions. Specifically targeting this vulnerable group, using group educational sessions with other food allergic adolescents might be an initial step in supporting this group. Use of technology-enhanced learning tools would be a potential way to engage as has been the case in other conditions

(316). It is necessary that communication between food allergic consumer and FE be improved. At clinic review, food allergic children and their parents must be encouraged to question staff concerning the risk of allergens, in addition to alerting staff of the child's FA. Communication aids such as role-plays or the use of technology -enhanced simulation scenarios that allow parents or children to simulate an encounter with staff from a FE virtually may help to equip them with skills useful in these settings in real life. As clinicians, we must continually seek the best way to prepare food allergic families to manage life-threatening anaphylaxis with regular education sessions. It is likely repeated educational opportunities online or in the form of videos will help reinforce skills taught during clinic face-to-face sessions. I am hopeful that the data collected regarding FA management in schools and preschool CCS will act as a catalyst to lobby for and inform the designing of a national schools policy on the care of Irish food allergic children. A gold standard FA policy would exist to support these facilities and be designed by all relevant stakeholders- parents, school staff, students, public health, general practioners and allergy specialists. The availability of stock adrenaline autoinjectors in schools would be a very positive step. In conjunction, training relevant staff in identification and management of AARs will be essential. We have shown how a novel written educational tool can have a significant effect on QoL, anxiety as well as self-efficacy in parents of young children with a new diagnosis of a nut allergy. If proven effective across larger more diverse populations, this cost neutral educational model could be used for a number of atopic conditions. I believe the future is bright for Irish food allergic children.

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