

RESEARCH PROJECTS

Using NHS Data to Monitor Trends in the Occurrence of Severe, Food-Induced Allergic Reactions Work Package 2

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FSA Research and Evidence

People with food allergies may experience food allergic reactions due to accidental exposure. These reactions are commonly categorised as non-severe, fatal food anaphylaxis and near-fatal food anaphylaxis. Non-severe allergic reactions to food are more common with an incidence of up to 1,000 times greater than fatal food-related anaphylaxis. However, obtaining accurate data relating to the circumstances under which these reactions occurred is challenging under the current diagnosis coding system used in the National Health Service (NHS).

This project addressed two key questions:

1. What are the trends in the occurrence of food hypersensitivity (FHS) reactions and their consequences in terms of healthcare encounters (both to hospital and primary care)?
2. What are the circumstances surrounding severe, life-threatening reactions to food?

Approach

- A UK arm of NORA was established using the same online platform as the existing European Registry.
- Participation of healthcare professionals and/or patients to enter relevant information was co-ordinated by BSACI in conjunction with the Paediatric Emergency Research in the United Kingdom & Ireland (PERUKI) network.
- Different versions of the questionnaire were developed to increase response rates: (1) a comprehensive form mapped to existing NORA data fields for completion by Healthcare Professionals in the non-acute setting; (2) a shorter form with key data

fields to increase data reporting in more pressured, acute healthcare settings; and (3) a form for completion by patients or their parent/guardian.

Key Results

The launch of the UK anaphylaxis registry faced delays and was impacted by significant pressures on NHS services due to the COVID-19 pandemic. This led to a lower than anticipated uptake of the Registry by clinics and Accident & Emergency departments. As a result, only a minority of accidental reactions (less than 5%) were captured in the registry, almost all in children and young people under age 18 years.

Some indicative results of this analysis are the following:

- 213 cases reported to be due to a food trigger and of these, 208 occurred in children/young people aged 18 years or under.
- Common food triggers were peanut, tree nuts (especially cashew), cow's milk/dairy and hen's egg.
- 47% of reactions occurred after consumption of prepacked food products and in at least 59% of these cases, the allergen was declared as an actual ingredient.

Further work would be needed to understand how to optimise reporting of data, for example by reducing the time burden for completion by clinicians and patients.

Abbreviations

A&E	Accident & Emergency
BSACI	British Society of Allergy & Clinical Immunology
CRN	Clinical Research Network
FHS	Food Hypersensitivity
FSA	Food Standards Agency
HCPs	Health Care Professionals
HRA	Health Research Authority
ICD	International Classification of Disease
NIHR	National Institute for Health and Care Research
NORA	Network of Online Reporting for Anaphylaxis
PERUKI	Paediatric Emergency Research in the United Kingdom & Ireland
PFAS	Pollen Food Allergy Syndrome
WAO	World Allergy Organization
WP	Work Package

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1. Lay summary

Previous estimates are that around 3-5% of the UK population have a food allergy. An analysis of national health data in England, commissioned by the UK Food Standards Agency, reported that from 2008 and 2018 the prevalence of food allergy was around 4% in preschool-aged children, 1-2% in school-aged children and 0.9% in adults.

People with food allergy are at risk of serious and potentially life-threatening allergic reactions (anaphylaxis). Allergic reactions due to accidental consumption are common in people with known food allergy. Unfortunately, there are limited data on the causes of accidental allergic reactions in the UK.

This project was designed to try and capture details regarding accidental allergic reactions to food. A voluntary online reporting system was established, to allow registered healthcare professionals to log reactions in patients presenting to health facilities in the UK for review, including the likely trigger and the circumstances of the reaction.

The most common food triggers reported were peanut, tree nuts (especially cashew), cow's milk/dairy and hen's egg. Anaphylaxis occurred in around half of cases reported. 47% of reactions were due to consumption of the allergen in prepacked food products and in many cases, the food was consumed despite the person having a known allergy to the ingredient and the ingredient being declared on the food label.

Unfortunately, reporting was compromised by the very significant pressures on NHS services in the UK. As a result, only a minority of accidental reactions (less than 5%) were captured, almost all in children and young people under age 18 years. In the context of previous attempts by the FSA to capture information relating to accidental reactions due to food allergy, it is unlikely that a voluntary reporting system will be effective. Other schemes should be considered, for example, mandatory reporting of anaphylaxis which has been introduced in Australia.

2. Executive summary

There is a general perception that food allergy is increasing in many countries, including in the UK. This is based on high rates of self-reported food allergy, and clear increases in surrogate measures such as prescription of low-allergy formula (for infants with possible milk allergy) or adrenaline autoinjectors (used to treat anaphylaxis reactions), or hospital admissions due to allergic reactions.

The consequences of a diagnosis of food allergy are significant. Food-allergic consumers must avoid the allergens to which they are allergic, something which often results in increased food costs. The diagnosis also impacts on social activities, and causes anxiety due to fear of potential reactions. Accidental reactions are common, and may be due to a variety of causes, including undeclared presence of food allergens in food products. It is therefore important to ensure that accurate data relating to the occurrence of accidental reactions are available, to help guide the need for "food alerts" to be communicated to the public, and possibly the need for food recalls.

Imperial College London was contracted by the Food Standards Agency (Contract Number FS101222) to establish a system for online reporting of accidental allergic reactions in the UK, in conjunction with the European Anaphylaxis Register (Network of Online Reporting for Anaphylaxis, NORA). After delays due to the COVID-19 pandemic, the Registry was launched in October 2021.

Between October 2021 and 27 August 2023, a total of 296 valid case reports were made to the Registry. This is likely to represent <5% of accidental reactions occurring in the UK. Overall, only 28 clinics and 11 Accident & Emergency (A&E) departments registered for access to the

platform. 213 (72%) were reported as being due to a food trigger, and of these, 208 (97.7%) occurred in children/young people aged 18 years or under.

Consistent with published data, the most common food triggers reported were peanut (14%), tree nuts (especially cashew) (26%), cow's milk/dairy products (20%) and hen's egg (12%). In around half of reports, symptoms reported were consistent with anaphylaxis. 47% of reported reactions were due to consumption of the allergen in prepacked food products; in at least 59% of these events, the allergen was declared as an actual ingredient on the food item. In a quarter of cases, the item was consumed despite the individual being known to be allergic to that particular allergen.

Unfortunately, the success of the Registry was impacted by a number of factors. These include the very significant pressures within the NHS system at the moment, exacerbated by the COVID-19 pandemic; the time-burden for reporting; issues with NHS IT infrastructure; confusion over the administrative requirements for a Research Database/Registry rather than clinical trials; and poor response rates by patients or their carers who were asked to submit further information online regarding the accidental reaction.

The Registry was therefore only able to capture a minority of accidental allergic reactions. The primary limiting factor was almost certainly the time burden on the part of clinicians to report cases in the context of a very time-pressured work environment.

Future approaches to collecting these data need to be as automated and integrated as possible. Finally, given the issues of voluntary reporting, it may be necessary to consider mandatory reporting of anaphylaxis (as is now being considered throughout Australia) in order to identify "near-miss" incidents and help inform the need for food recalls among other public health measures.

3. Project outline

Imperial College London was contracted by the Food Standards Agency (Contract Number FS101222) to undertake research to use existing NHS datasets to better understand trends in food hypersensitivity (FHS) reactions, and in particular, food-induced anaphylaxis, in the UK.

Specifically, the project's objectives were to:

- i. Assess the available data relating to NHS encounters (hospitalisations, visits to healthcare facilities including primary care and Accident & Emergency departments) due to FHS, in order to evaluate trends in healthcare visits for FHS in England (and where data is available, for the devolved nations).

- ii. Attempt to validate the different codings used in primary and secondary care for FHS, to guide future use of NHS datasets to monitor trends in epidemiology.
- iii. Establish a prospective registry for food and non-food related anaphylaxis in the UK, in partnership with the European Anaphylaxis Registry.

This report presents the results and analysis from objective (iii), to help inform future FSA activities.

4. Introduction

Food allergy continues to attract significant attention at a public health level and in the media. It is the commonest cause of potentially life-threatening allergic reactions (anaphylaxis), a serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death (Turner et al., 2019). The consequences of a diagnosis of food allergy are significant. Food-allergic consumers must avoid the allergens to which they are allergic, something which often results in increased food costs – both direct and indirect (for example, increased time needed to shop for “safe” options). The diagnosis also impacts on social activities, and causes anxiety due to fear of potential reactions.

Food allergy is not the same as food intolerance: food allergies are caused by the immune system reacting to an otherwise harmless food protein, something known as an *allergen*. The type of food allergy that can cause life-threatening reactions (anaphylaxis) involves the Immunoglobulin E (IgE) antibody which recognises the food allergen and triggers an immune response. IgE-mediated food allergy is the most common immune-mediated FHS in children and adults.

Food allergy – especially that caused by the IgE antibody – triggers an immune response (similar to a domino effect) which can cause symptoms of an allergic reaction, ranging from mild itchy skin itch to life-threatening reactions ([Figure 1](#)). Anaphylaxis is a serious allergic reaction which lies along this spectrum of severity.

The World Allergy Organisation (WAO) defines anaphylaxis as “a serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterised by potentially life-threatening compromise in airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present” (Cardona et al., 2020). Most anaphylaxis reactions are self-limiting, however severe anaphylaxis reactions are unpredictable – so everyone with IgE-mediated food allergy must be managed as potentially being at



Mild, localized
symptoms

Generalized allergic
reaction

Anaphylaxis

Severe
anaphylaxis

Figure 1. Symptoms due to a food-induced allergic reaction lie on a spectrum of severity, ranging from mild localised symptoms (e.g. itchy mouth) to near-fatal (and even fatal anaphylaxis).

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risk of severe reactions. For example, individuals at risk of food-induced anaphylaxis are normally prescribed adrenaline autoinjector “pens” to be used in the event of anaphylaxis.

IgE-mediated food allergy is widely accepted to be increasing in many regions of the world – by the public, healthcare professionals and scientists (Sampath et al., 2021; Simons & Sampson, 2008). This is based on high rates of self-reported allergy, and clear increases in surrogate measures such as prescription of hypoallergenic formula products or adrenaline autoinjector “pens”.

As part of a contract with the Food Standards Agency (Contract Number FS101222), Imperial College London undertook an analysis of national health datasets in England from 2008 to 2018, and found that the prevalence of food allergy was around 4% in preschool-aged children, 1-2% in school-aged children and 0.9% in adults. However, aside from data related to fatal anaphylaxis reactions (Baseggio Conrado, Ierodiakonou, et al., 2021), there is very limited information in the United Kingdom as to the specific foods responsible for food allergies, and in particular, those causing accidental reactions in susceptible individuals. This is in contrast to many European countries, where an Anaphylaxis Registry was established in 2011.

The aim of this project was to establish a voluntary register for reporting of anaphylaxis by healthcare professionals in the UK, and evaluate uptake and cases reported.

5. Methods

Working together with the European Anaphylaxis Register (Network of Online Reporting for Anaphylaxis, NORA) led by Prof Margitta Worm (Charité Hospital, Berlin), a prospective anaphylaxis register was

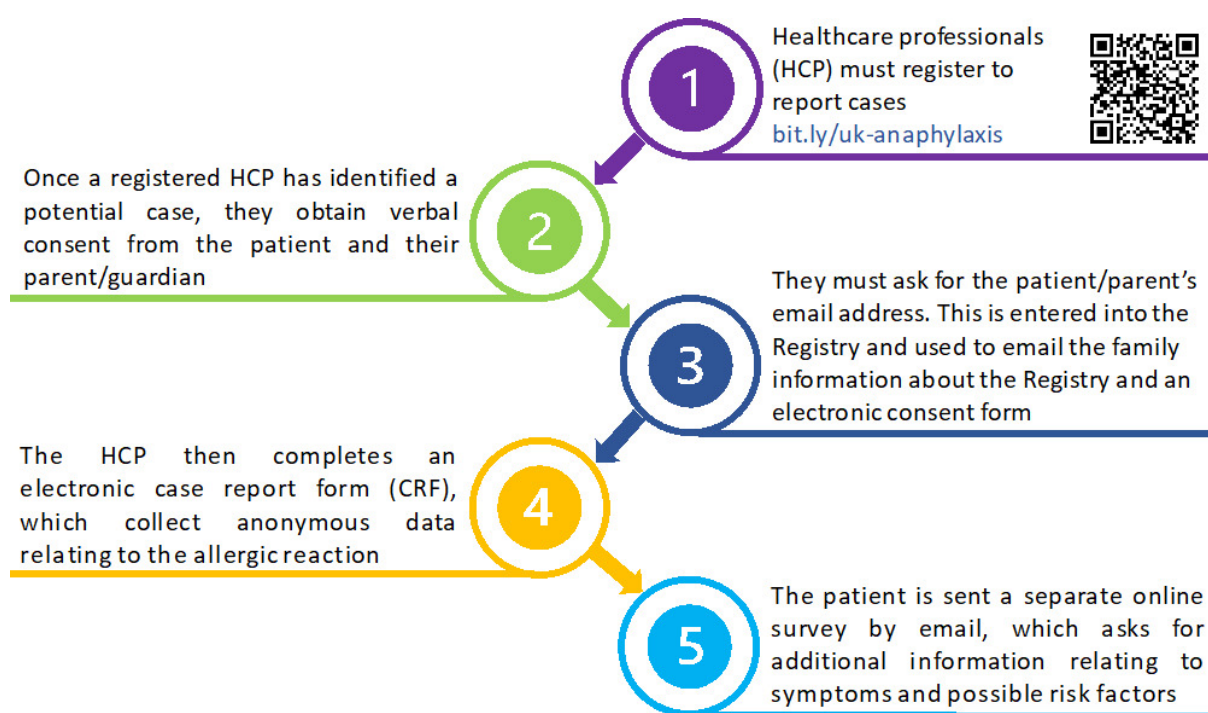


Figure 2. Schemata for the reporting of reactions

established for food and non-food related allergic reactions in the UK, with the support of the British Society for Allergy and Clinical Immunology (BSACI).

The Registry was originally intended to commence in April 2020, however this was delayed as a result of the COVID-19 Pandemic. The Registry was launched in October 2021, to coincide with the BSACI Annual Meeting. The Registry was approved by the NHS Human Research Authority (reference 21/LO/0259) as a National Research Database.

The Registry was publicised through the BSACI, as well as in conjunction with the Paediatric Emergency Research in the United Kingdom & Ireland (PERUKI) network. Healthcare professionals first had to register, following which they were provided with access to the online reporting platform, as shown in [Figure 2](#). Verbal consent was obtained from the patient (or their parent/guardian).

5.1. Eligibility criteria for cases

Any episode of a significant allergic reactions (not just anaphylaxis) occurring in the community following unintended allergen exposure (irrespective of whether the trigger is food) was eligible for entry into the Registry.

The allergic reaction must have occurred within the last 12 months and not have been caused by food/drug challenges conducted in hospital/clinic.

5.2. Case reporting

Two data collection forms were established: a full reporting form for non-acute environments (see Section 9, Appendix 1) and a shorter form for acute environments such as Accident & Emergency (A&E) departments (see Appendix 2).

5.3. Timeline for reporting

The first case was reported in May 2022. This report details all completed, reported cases up to and including 27 August 2023.

6. Results

Between October 2021 and 27 August 2023, a total of 296 valid case reports were made to the Registry; the first report was made on 4 May 2022, which equates to an average of 19 reports per month. Overall, 28 clinics and 11 A&E departments registered for access to the platform. There are approximately 170 A&E departments in the UK, so only a minority participated in the Registry.

113 (38%) reports were completed by A&E staff, usually around the time of reaction. The remainder were completed in follow-up settings (37% hospital allergy clinics, 28% general paediatric clinics). With respect to case reports made outside Emergency Departments, the median time to report was 81 days (see [Figure 3](#)).

Of the 296 case reports, 213 (72%) were reported as being due to a food trigger. In the 42 reports where a non-food trigger was identified, 22 (52%) were due to medication (12, antibiotics; 2 ibuprofen; 2 following immunisation); 2 venom; 18 to possible environmental exposures (pets, pollen, creams, washing powder). No obvious acute trigger was declared in 41 (14%) of reports, of which 34 of 41 reactions involved angioedema/urticaria which can be viral or immune in aetiology.

The response rate to the patient/carers follow-up questionnaire was 19% for those cases initially reported in A&E departments, and 24% for those cases reported by non-emergency staff.

6.1. Reported cases due to a food trigger

213 case reports were received where a food trigger was suspected to be the cause of the allergic reaction. 208 (97.7%) of reported reactions occurred in children/young people aged 18 years or under (see [Figure 4](#)). There was a slight predominance on reactions in male versus female children prior to the age of puberty, in line with previous observations where food allergy is slightly more common in prepubertal males compared to females (Afify & Pali-Schöll, 2017).

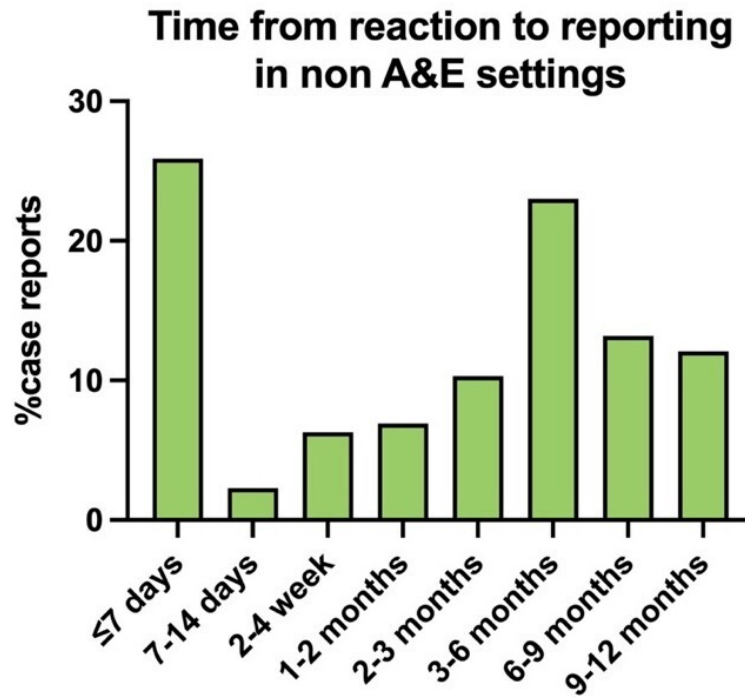


Figure 3. Time from reaction to reporting with respect to reactions reported outside A&E settings

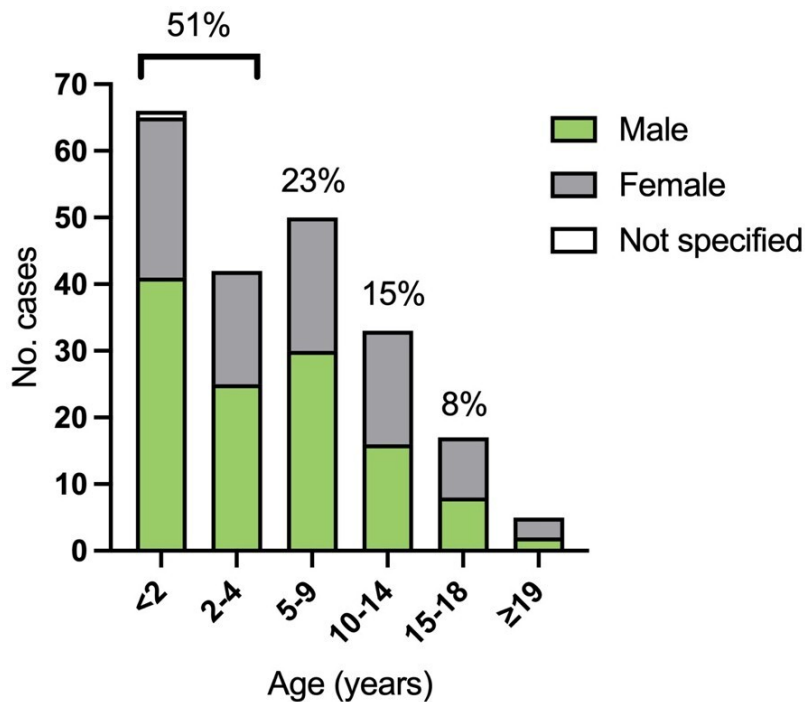


Figure 4. Age/gender distribution of cases reported due to a food allergen

Self-reported ethnicity was available in 49 cases: 28 (57%) reported “White British” background; 4 (8%) “White-other”; 8 (16%) reported “African, Caribbean, any other Black/African/Caribbean background”; 3 (6%) reported “Asian” background; 6 (12%) “mixed White/Asian” background.

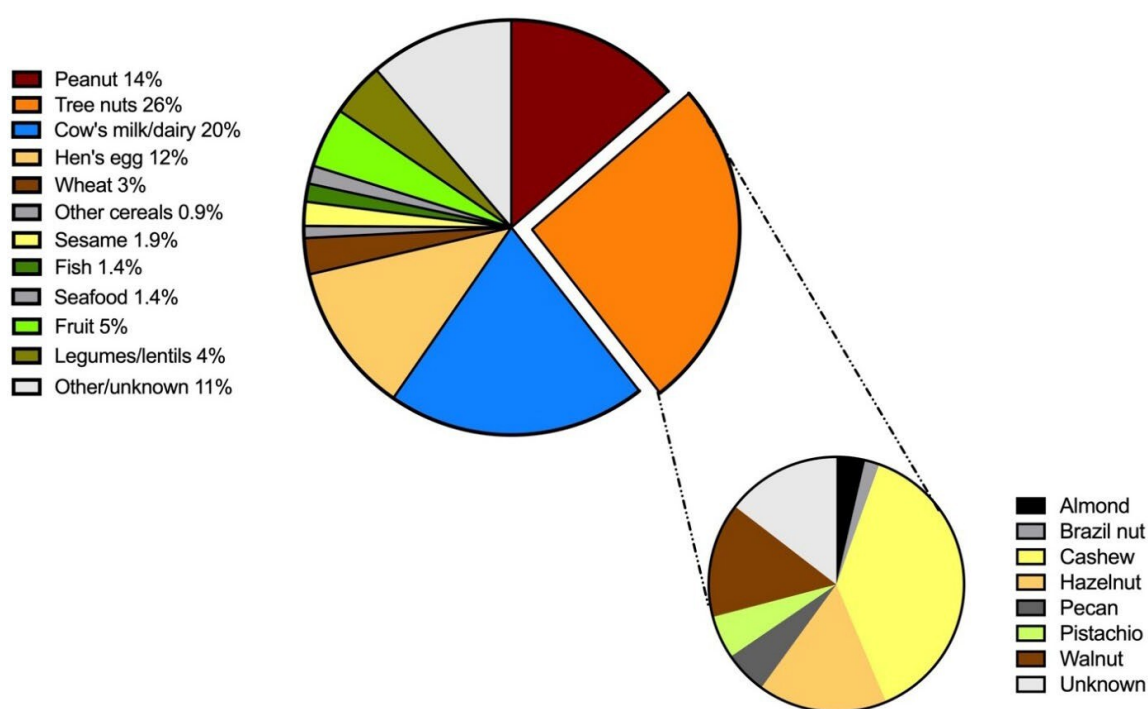


Figure 5. Reported food triggers

Due to the limited data available relating to ethnicity, it was not possible to assess whether the cohort is representative of the wider, food-allergic population.

6.2. Reported triggers

Reported triggers are shown in [Figure 4](#) and [Table 1](#). Peanuts and tree nuts/seeds together accounted for 89 (42%) reactions, with 29 (14% of the total) due to peanut and 55 (26%) due to tree nuts. The most common tree nut implicated was cashew (causing 21 of 55 reactions), followed by hazelnut (9 reactions) and walnut (8 reactions).

In children under 2 years, the most common triggers were hen's egg and cow's milk, together accounting for around one half of reactions ([Figure 5](#)).

Table 1. Reported food triggers

Food allergen	No. reports	Percentage of total reports
Peanut	29	14%
Tree nuts		26%
• Cashew	21	10%
• Pistachio	3	
• Hazelnut	9	4%
• Walnut	8	4%
• Pecan	3	
• Almond	2	
• Brazil nut	1	
• Unspecified/unknown	8	

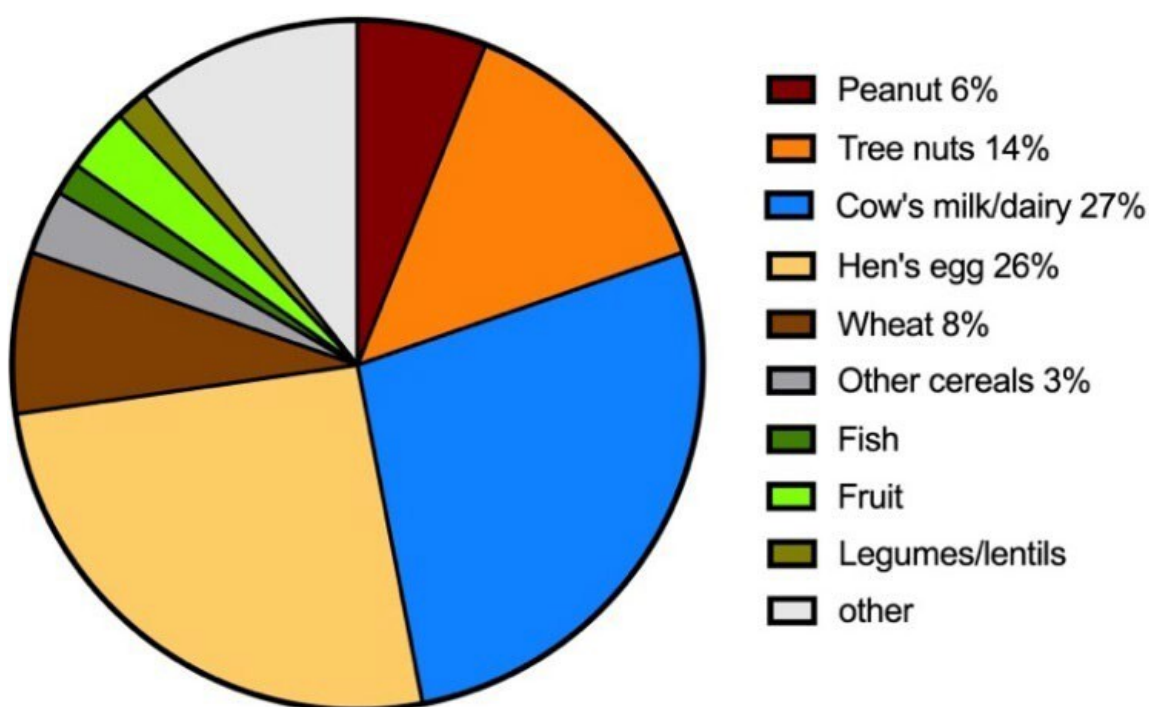


Figure 6. Reported food triggers in children under 2 years of age

Food allergen	No. reports	Percentage of total reports
Cow's milk / dairy	43	20%
Hen's egg	25	12%
Cereals		
• Wheat	6	3%
• Other/unknown	2	0.9%
Sesame	4	1.9%
Fish	3	1.4%
Seafood	3	1.4%
• Prawns	2	
Fruit		5%
• Apple	1	
• Banana	1	
• Cherry	1	
• Date	1	
• Kiwi	1	
• Raisins	1	
• Strawberry	2	
• Unknown	2	
Pulses (legumes excl. peanut)		4%
• Pea	4	
• Soya	3	
• Chickpea	1	
• Lentils	1	
Other/unknown	24	
TOTAL	213	100%

Children under 2 years were less likely to present with reactions to peanut or tree nuts, and more likely to present with reactions to hen's egg and wheat. Cow's milk accounted for 20% of reactions overall, 27% of reactions in children under 2 and 12% of reactions in participants aged 11+ years (see [Table 2](#)).

Limiting reports to the 73 cases presenting to A&E departments acutely, the most common triggers were: peanut (15%), tree nuts (26%), hen's egg (16%), cow's milk/dairy (14%) ([Table 2](#)).

Table 2. Reported food triggers in participants under 2 years, and in those presenting acutely to Accident & Emergency

Food allergen	No. cases (all ages)	No. cases in <2 years	No. cases presenting to A&E
Peanut	29 (14%)	4 (6%) p<0.05	11 (15%) Not sig.
Tree nuts	55 (26%)	9 (14%) p<0.01	19 (26%) Not sig.
Cow's milk / dairy	43 (20%)	18 (27%) Not sig.	10 (14%) Not sig.
Hen's egg	25 (12%)	17 (26%) p<0.01	12 (16%) p<0.05
Wheat	6 (3%)	5 (8%) p<0.01	2 (3%) Not sig.
Fish + seafood	6 (3%)	1 (2%) Not sig.	2 (3%) Not sig.
Other	49	12	17
TOTAL	213	66	73

P values calculated according to Fisher Exact test.

6.3. Circumstances surrounding the exposure

Data regarding the circumstances of the exposure were available in 130 cases. In 4 cases, the reaction was reported to occur without actual ingestion (i.e. due to contact [3 reports] or inhalation of fish vapours [1 report]).

Location of reaction: 7 (5%) reactions occurred while abroad on holiday. 73 (56%) occurred at home, 11 (8%) in a friend/relative's home, 16 (12%) at a place of education, and 12 (9%) at a restaurant or similar outlet (see [Figure 6](#)).

Source of allergen: In 61 reactions (47%), the food containing the allergen was a prepacked food item. In at least 36 cases, the allergen was declared on the food packet as an ingredient. Fifteen individuals had previously reacted to the causative allergen before: in 10 of these 15 reports, the ingredients were not checked prior to eating. In 53 of 61 (87%) cases, the amount consumed was less than one mouthful, something which may be due to the rapid onset of symptoms reported in 41 of these 61 cases.

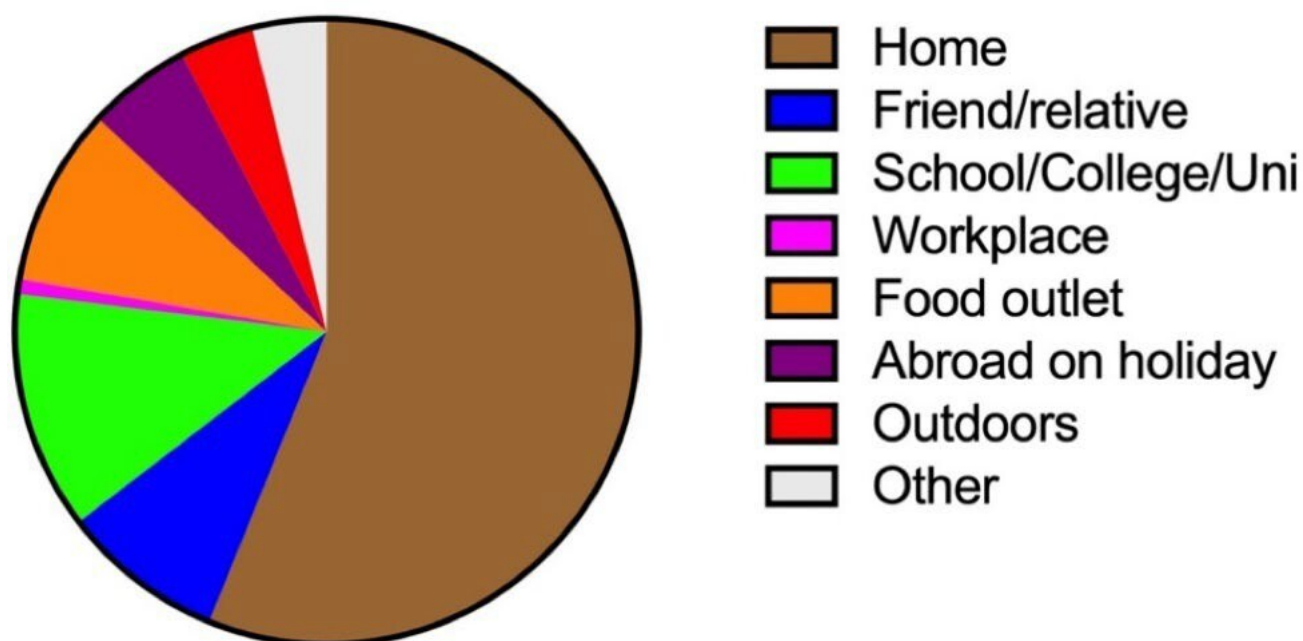


Figure 7. Location of reaction

For the other 69 reports (where the reaction was not due to a prepacked food, and thus the food product might not have had a clear ingredients list on the packaging), the food product was obtained from a variety of sources: restaurants and other food outlets (10), supermarkets (6), entertainment venue (1), other/not declared (52).

Overall, 61 (47%) of reactions occurred to a known allergen for that individual. In 19 cases, the ingredients were not checked prior to consumption, while in 10 cases, the ingredients were checked but presence of the allergen not noted.

Factors which might have impacted upon severity of reaction: Co-factors such as intercurrent viral infection or recent exercise have been reported to sometimes affect the severity of an allergic reaction. In 172 (81%) of reactions, no obvious co-factor was identified. In 41 reactions, at least one possible co-factor was identified. 17 individuals had an intercurrent infection; 10 had undertaken recent exercise. No individuals were taking medication at the time of reaction that might act as a co-factor, but this probably reflects the fact that the vast majority of cases included occurred in children and young people.

6.4. Symptoms experienced during the allergic reaction

Symptoms experienced included skin (89%), gastrointestinal (59%) and respiratory (63%). Reactions involved the skin only in 18% of reactions. Thus, the majority of reactions (80%) involved more than one organ system.

Symptoms consistent with anaphylaxis (WAO definition) were present in 105 (49%) of cases. The five most common triggers for these events were: peanut, 14 (13%); tree nuts, 27 (26%); cow's milk, 26 (25%); hen's egg, 9 (9%); wheat 5 (5%). The proportion of anaphylaxis due to these specific allergens was not statistically different from those causing reaction of *any* severity (Fisher Exact test).

Emergency medical services were contacted in 94 (44%) of all reactions, and 55 (52%) of anaphylaxis reactions. Adrenaline was administered in 73 (34%) of all reactions, and 48 (46%) of possible anaphylaxis reactions. 18 reactions required more than one dose of adrenaline (given by a healthcare professional in 15 cases). One patient (with a reaction triggered by cow's milk) was commenced on an intravenous adrenaline infusion and admitted to intensive care. In total, 109 (51%) of presentations were associated with a hospital admission. There were no fatalities.

7. Discussion

The reporting system established in this research tender attempted to collect data to help the FSA better understand the causes and circumstances of unintended allergic reactions to food occurring in the UK.

Consistent with published data, the most common food triggers reported were peanut, tree nuts (especially cashew), cow's milk/dairy and hen's egg (Baseggio Conrado, Patel, et al., 2021). In around half of reports, symptoms reported were consistent with anaphylaxis. 47% of reported reactions were due to consumption of the allergen in prepacked food products; in at least 59% of these events, the allergen was declared as an actual ingredient on the food item. In a quarter of cases, the item was consumed despite the individual being known to be allergic to that particular allergen.

The FSA commissions a biannual survey called "Food and You" to measure consumers' self-reported knowledge, attitudes and behaviours related to food safety and other food issues amongst adults in England, Wales, and Northern Ireland. The last survey ("Wave 6") was conducted between 12th October 2022 and 10th January 2023. A total of 5,991 adults (aged 16 years or over) from 4,217 households completed the 'survey. Within the survey, respondents are asked as to whether they have FHS or food allergies. The most common self-reported triggers for allergic reactions in "Wave 6" were: fruit (29%), tree nuts (23%), peanut (21%), crustacea (17%) and molluscs (10%) (Armstrong et al., 2023). The most obvious difference between the "Wave 6" survey and this report is that fruit was a more common reported trigger, while cow's milk was not identified as a major trigger in the "Food and You" survey. This may be because "Food and You" is a self-reporting survey completed by respondents over 16 years of age while in this project, the vast majority of allergic reactions reported were in children and young people.

Cow's milk is increasingly seen as the culprit allergen for fatal food reactions in the UK (Baseggio Conrado, Ierodiakonou, et al., 2021), and is now the commonest cause of fatal anaphylaxis in children. Consistent with data from the European Anaphylaxis Register (Grabenhenrich et al., 2016), cow's milk was a common trigger for accidental reactions, accounting for one in five reactions. More education is needed to highlight the specific risks posed by cow's milk to allergic individuals, to increase awareness amongst food businesses (Grabenhenrich et al., 2016). Many individuals with an allergy to a fruit have a secondary food allergy, where symptoms are caused by similarities between proteins in fruit and pollens: this is known as Pollen Food Allergy Syndrome (PFAS), where sensitive individuals essentially experience "hay fever" symptoms in the mouth and throat. More severe reactions and anaphylaxis are less common in PFAS, because the proteins are readily broken down by stomach acid and thus less likely to trigger systemic reactions (Skypala et al., 2022). These differences demonstrate that using data relating to allergic triggers obtained through "Food and You" may not be a reliable guide in terms of policy.

Legislation currently requires declaration of 14 "priority" allergens when present as an ingredient in prepacked food items. These 14 allergens are: celery, cereals containing gluten (such as wheat, barley and oats), crustaceans (such as prawns, crabs and lobsters), eggs, fish, lupin, milk, molluscs (such as mussels and oysters), mustard, peanuts, sesame, soybeans, sulphur dioxide and sulphites and tree nuts (such as almonds, hazelnuts, walnuts, brazil nuts, cashews, pecans, pistachios and macadamia nuts). It is concerning that at least one quarter of accidental reactions to prepacked foods in those with a known food allergy occurred despite the allergen being declared on the ingredients. Michelsen-Huisman et al (2018) undertook a prospective study of 157 adults in the Netherlands with a physician-confirmed diagnosis of food allergy. During a 1-year follow-up, 73 patients reported 153 accidental allergic reactions. 62 (41%) were due to prepackaged foods, and labelling information was available in 52 cases. In 33 (63%), the suspected allergen was declared as an ingredient on the label. However, patients only read the label two thirds of the time. Reasons for not reading the label included illegible writing, having eaten the food before or a general perception that "I didn't expect allergens in the product" or "I thought that it was safe" (Michelsen-Huisman et al., 2018). These data flag the importance of allergic individuals (and those providing food for them) to carefully read ingredients on prepacked foods.

Unfortunately, the success of the Registry was impacted by a number of factors. First, the launch of the Registry was delayed by the COVID-19 pandemic. Notwithstanding, the Registry was launched in October 2021, at a time when social distancing precautions were still in place in healthcare facilities. Whether the additional burden on healthcare workers in the UK resulted in the limited uptake of the reporting system by healthcare

workers is unclear, although anecdotal reports imply this was a major barrier. Overall, only a minority of allergy clinics and A&E departments contributed cases during the study period, despite the Registry being adopted to the National Institute for Health and Care Research (NIHR) portfolio which provided limited resource to local centres in England for reporting cases.

Case reporting was originally intended to take a maximum of 10 minutes. The platform logged the start and completion time for each case report; in some cases, reporting took significantly longer (hours or even days), implying that the report was not completed in “one sitting”. Limiting the analysis to reports where completion time was less than 1 hour, completion took a mean of 17.5 minutes (standard deviation of 12 minutes), with the shortest completion time just over 3 minutes. 34% of reports were achieved in under 10 minutes. Clearly, in acute settings, there was a need to reduce the time burden for completion. An abbreviated form was therefore developed, which reduced the mean completion time to 9 ($\pm$ 8 minutes), with 75% of reports achieved in under 10 minutes and 30% in under 5 minutes. A number of further efficiencies were built into the system, to allow the case reporting to directly export some text which could be included in any discharge summary or referral. In addition, paper forms were designed which could be completed more rapidly if online access was not readily available. Despite this, there was a clear time-burden (or at least a perception of burden) which is almost certainly likely to have hampered uptake, at a time when acute NHS provision was already under great pressure.

There were also some unexpected obstacles. In many hospitals, the reporting website was blocked by NHS firewalls; although this could frequently be solved, the additional work required seemed to reduce enthusiasm in some centres. An additional complication was the inconsistent classification of the Registry by different NHS organisations. The approval from the NHS Health Research Authority allowed for the Registry to collect de-identified data from participants with verbal consent, and without formal agreements between the NHS site and the Sponsoring organisation (as would be required for clinical trials). However, a number of NHS organisations were unfamiliar with this arrangement for Research Databases; in some cases, this served as an impediment to clinicians participating in the Registry.

Finally, one of the key features of the Registry was to combine data collection from both healthcare professionals (to minimise the risk of false or inappropriate reports) and from the affected food-allergic person (or their carer). The intended aim was to compare clinician versus self-reported details, to inform future work. In particular, the abbreviated form,

used in acute settings such as A&E, depended on the circumstances of the reaction being reported by the food-allergic individual (or their carer) directly.

Disappointingly, this only occurred in 19% of cases. The low response rate precluded this planned analysis.

As a result, it is difficult to determine the degree to which the data obtained are representative of the UK population. Only 2% of reported cases occurred in adults; this is likely to be a function of the far greater (but still limited) provision of allergy clinics in paediatric compared to adult settings, as well as the absence of a research network in the UK for adult A&E departments (in contrast to the PERUKI network of Children's A&Es). Even so, there are at least 118 allergy clinics in the UK (data from BSACI), thus only a minority reported cases. A separate analysis of NHS data has estimated that there are around 2700 hospital admissions due to food allergy in the UK, annually (Baseggio Conrado, Ierodiakonou, et al., 2021): the dataset therefore only captured around 3% of estimated hospital admissions due to accidental allergic reactions to food, and up to 7% of those in children under 15 years. Nonetheless, as noted above, the causes and circumstances of reported reactions are not dissimilar to previous reports.

These issues highlight the challenges faced by health and regulatory agencies when collecting data of this nature. Unless there is significant incentive, it is difficult to persuade busy clinicians working in time-pressured environments to take on additional tasks, or even food-allergic individuals who themselves have experienced an allergic reaction (or those caring for them). Recent coronial inquests have highlighted a need to improve data collection relating to accidental food reactions. This Registry was one mechanism assessed by the FSA to improve data collection in this area, and achieve greater clarity over food incidents related to allergy and the need for food recalls. The FSA recently undertook proof-of-concept testing of an online reporting tool (food allergic reaction reporting mechanism, FARRM) to enable consumers to self-report allergic reactions from November 2021 to February 2022. A number of potential issues were highlighted with respect to data validity, and consumer and stakeholder expectations for data sharing. There were also wider considerations as to how consumer awareness and motivation to use the tool could be sustained over the long term, leading to the conclusion that "alternative methods of collecting data on the nature and number of FHS reactions and near misses should be explored." (FSA, 2022).

An alternative approach is that adopted by the State of Victoria in Australia (<https://www.health.vic.gov.au/public-health/anaphylaxis-notifications>.) In 2013, a 10- year-old boy died following consumption of a can of imported coconut drink which failed to declare the presence of milk as an ingredient

on its label. At the time, the hospital was not required to notify local authorities and as a result, the product remained in shops for six weeks before being recalled. To avoid this from happening again, mandatory reporting of anaphylaxis in public hospitals was instituted state-wide in November 2018 – analogous to the reporting of communicable diseases which are considered to be associated with a public health risk.

Of concern, there are many similarities between this case and the death of Celia Marsh who died in 2017 having eaten a vegan product which contained undeclared milk protein in a dairy-free coconut yogurt alternative. Concerns were raised by the Coroner with respect to delays in “the immediate investigation into a suspected death from anaphylaxis” which also resulted in a delayed recall of the product. The Coroner specifically recommended the establishment of “a robust system of capturing and recording cases of anaphylaxis, and specifically, fatal and near-fatal anaphylaxis, to provide an early warning of the risk posed to allergic individual by products with undeclared allergen content. Such a system could involve mandatory reporting of anaphylaxis presenting to hospitals, analogous to the current system used for notifiable diseases (including some food-borne illnesses) whereby registered medical practitioners have a statutory duty to notify the ‘proper officer’ at their local council or local health protection team of suspected cases of certain infectious diseases. An example of such a reporting system for anaphylaxis already exists in the state of Victoria in Australia, and also allows for rapid alerts of serious cases to public health authorities to expedite investigation and evaluate the public health risk.” (Voisin, 2022).

Given the experience of voluntary reporting systems in the UK, the Australian approach may be one that needs to be considered if more comprehensive data relating to accidental reactions to food are to be collected. Importantly, if such an approach is considered in the UK, it would require provision of an appropriate online reporting system to reduce the time burden for completion to an absolute minimum.

Unfortunately, existing hospital data systems in the NHS do not collect information relating to the cause of food-induced allergic reactions. Current NHS datasets are incomplete and very prone to miscoding (Turner et al., 2015). Hospital visits are currently coded according to the International Classification of Disease (ICD)-10 system; this has a number of limitations which have been outlined elsewhere (Tanno et al., 2017, 2020). These include miscoding of non-acute visits to hospital for food allergy, for which a new code (Z91.01) was introduced in 2016, but not in the UK. The planned introduction of ICD-11 coding will hopefully address many of the current limitations of ICD-10 (Tanno et al., 2020) – for example, the inclusion of the causative allergen as part of the coding. Unfortunately, a proposal to include a classification of anaphylaxis by clinical severity

was rejected (Tanno et al., 2017). It is not inconceivable that a system could be established in the UK where the correct identification of cases through appropriate ICD coding could trigger an email link to be sent to food-allergic individuals (or their carers) prompting them to submit further details of accidental reactions via an online form, thus minimising the time-burden on clinicians. However, given the low response rate in reporting by affected individuals in this Registry, further work would be needed to understand how to optimise direct reporting of data by patients.

7.1. Conclusions and policy implications

Despite the limitations of this dataset, we did not identify any significant differences between the causes of accidental food reactions logged and that reported in the literature. Of concern, a significant proportion of reactions occurred due to consumption of prepacked foods, despite the allergen being declared as an ingredient on the product.

The Registry was only able to capture a minority of accidental allergic reactions occurring during the study period. The primary limiting factor was almost certainly the time burden on the part of clinicians to report cases in the context of a very time-pressured work environment, particularly in the post-covid era. Even if the time burden for reporting can be reduced to under 5 minutes, as was often the case with the abbreviated report for A&E departments, it is unlikely that uptake would be significantly improved given the lack of integration between different computer systems. Future approaches to collecting these data need to be as automated and integrated as possible. Finally, given the issues of voluntary reporting, it may be necessary to consider mandatory reporting of anaphylaxis (as is now being considered throughout Australia) in order to identify “near-miss” incidents and help inform the need for food recalls among other public health measures.



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Appendix

Case report form

UK Anaphylaxis Registry: Paper case report form for A&E and GPs

This form is for staff working in A&E or Primary care settings only. Document ONE reaction per form, for any unintended allergic event in adults and children, irrespective of whether the reaction was anaphylaxis. ALL fields are mandatory. Once completed, please enter data on to the Registry platform (anaphylaxis.net). Remember to for verbal consent and for the patient (or parent/guardian) to provide their email address (needed for them to receive an electronic consent form).

Patient Information		Date of reaction	Patient age	Sex at birth
Verbal consent agreed (Yes/No)		Patient's email address		
Section 1. About the allergic reaction		1.1 What symptoms occurred? Please circle <u>all</u> that apply		
Skin and mucosal	None	Angioedema (incl. swollen lips/ face)	Pruritus/ itch	Urticaria
		Erythema/ flush	Conjunctivitis	Unknown
Gastrointestinal	None	Abdominal pain/ cramps	Diarrhoea	Nausea
		Abdominal distension	Dysphagia	Faecal incontinence
				Unknown
Respiratory	None	Rhinitis	Throat tightness	Stridor
		Dyspnoea/SOB	Chest tightness	Vocal hoarseness
		Cough	Wheezing (expiratory)	Laryngeal oedema
				Unknown
Cardiovascular	None	Dizziness	Loss of consciousness	Tachycardia
		Palpitations/ arrhythmia	Hypotension (collapse)	Bradycardia
		Less alert (floppy in babies)	Chest pain/angina	Cardiac arrest
				Unknown
Other		Dysarthria	Hotness	Sweating
		Paraesthesia	Sight disorder	Trembling
			Feeling of impending doom	Tingling/burning of the hands/feet
				Cyanosis
				Pallor
Please rate symptom severity from <u>your</u> perspective, for each of the following (1=very mild, 10=very severe)				
SKIN:	GUT:	ENT:	RESP:	CVS:
				OVERALL:
1.2 What do you estimate was the time between allergen exposure and first symptoms? []				
1.3 Was there a biphasic reaction? ☐ No ☐ Unknown ☐ Yes: how long after initial reaction? (hrs) []				
1.4 For fatal reactions only				
Time from exposure to death: []				
Treatment given prior to arrest? ☐ Yes ☐ No ☐ Unk Adrenaline given prior to arrest? ☐ Yes ☐ No ☐ Unk				
Section 3. Eliciting factors				
3.1 Is the suspected allergen known? ☐ Yes ☐ No ☐ Reasonable suspicion				
For food allergens only		For other eliciting factors only		
3.2 Which food caused the reaction? Specify: []		3.4 Which other eliciting factor caused the reaction, please choose <u>one</u> :		
		☐ Insect Venom, which []		
		☐ Latex		
		☐ Specific immunotherapy (SIT)		
		☐ Exercise as the cause for anaphylaxis, in the absence of any other factor		
		☐ Temperature e.g. heat/ cold-induced symptoms		
		☐ Other eliciting factors, if not specified above		
For drug allergens only				
3.3 Which drug caused the reaction? Specify: []				
Section 4. Exacerbating factors and diseases				
4.2 Might the following conditions have contributed to reaction severity? Tick <u>all</u> that apply				
☐ An acute infection (e.g., common cold, flu)		☐ Hormone-based contraception / hormone replacement therapy		
☐ Physical exercise as co-factor/ exacerbating factor		☐ Alcohol		
please circle: mild/ moderate/ vigorous/ unknown		☐ Sleep deprivation		
☐ Psychological stress		☐ Other cofactors: please specify		
☐ Drugs: please specify []		☐ None identified/ unknown		
☐ Menstruation				

UK Anaphylaxis Registry
IRAS ref: 284011

Paper version of Case Report Form V1.0 20Jun2022
REC ref: 21/LO/0259

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Contact: anaphylaxis.registry@npsa.nhs.uk

Abbreviated case report form for acute settings