

REGULAR ARTICLE

A 10-year review found increasing incidence trends of emergency egg allergy reactions and food-induced anaphylaxis in children

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Keywords

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ABSTRACT

Aim: International reports have suggested that food allergies and food-induced anaphylaxis have increased in children. We investigated the incidence of emergency food reactions over a 10-year period.

Methods: This study retrospectively reviewed the medical records of children presenting to Umeå University hospital, Sweden, with an emergency food reaction from January 1, 2006 to December 31, 2015. Cases were identified using discharge codes for allergies and anaphylaxis. Anaphylaxis cases were included if they fulfilled the international criteria.

Results: We found emergency food allergy reactions in 519 children (58% boys) from 2006–2015 at a median age of 1.3 years. One-third were hospitalised (32%) including 71/99 cases of anaphylaxis. Milk and eggs were the most commonly identified triggers. Emergency reactions to eggs increased during the study period with a Spearman rank correlation coefficient of 0.770 ($p < 0.01$) and the figures for anaphylaxis were 0.745 ($p = 0.013$). The incidence of food-induced anaphylaxis increased and was 30 per 100 000 person-years for the study period.

Conclusion: Most of the emergency reactions, treated by secondary care paediatricians and emergency physicians, were to milk and eggs. Allergic reactions to eggs increased from 2006 to 2015, as did food-related anaphylaxis.

INTRODUCTION

The global incidence of food allergies and food-induced anaphylaxis in children and adolescents appear to have increased during the last few decades (1–4). Milk and egg allergies are most common in young children, affecting 2–3% and 0.5–2.5% worldwide, respectively (5–7). Allergies to peanuts, tree nuts and fruits are most common in adolescence (5) with varying prevalence and incidence rates, depending on the region they live in. Studies from southern Sweden have reported that the most common food triggers leading to paediatric emergency visits were milk, eggs, peanuts and tree nuts (8,9). The incidence of allergic reactions to cashew nuts, in particular, showed an increasing trend during a 10-year review from 2001 to 2010 (8).

Food allergy reactions include the whole spectrum, from mild, local reactions to systemic life-threatening conditions such as anaphylaxis. The absence of a universally accepted definition of anaphylaxis is one factor that has hindered attempts to establish the population-based incidence. In 2006, new international criteria for anaphylaxis were

suggested (10). The triggers for anaphylaxis differ according to age, but food is the most common cause in children (11) and it is notable that children under four years of age have been reported to have the highest incidence of food-triggered anaphylaxis (12).

The incidence of paediatric emergency food allergy reactions has not been described in northern Sweden to date and it is yet unknown if the incidence of food allergy reactions, including anaphylaxis, has increased in our region. Our previous data from northern Sweden suggested that children at risk of anaphylaxis may not have been prescribed adrenaline auto-injector devices to the extent required (13). The aim of this study was to investigate the

Abbreviations

FPIES, Food protein-induced enterocolitis syndrome; ICD-10, International Statistical Classification of Diseases, Tenth Revision; IgE, Immunoglobulin E.

Key notes

- The incidence of paediatric emergency food allergy reactions and anaphylaxis appear to have increased globally and this single site study examined 519 cases over a 10-year period.
- This paper reports that emergency egg allergy reactions and food-induced anaphylaxis increased in children from 2006 to 2015 at a university hospital in northern Sweden.
- One-third of the children were hospitalised (32%), including 77/99 cases of anaphylaxis.

trends in the incidence of emergency food reactions in children and adolescents by describing the number of paediatric emergency visits to Umeå University hospital during a 10-year period. We also characterised the cases epidemiologically with regard to sex, age, food triggers, symptoms and emergency treatment.

MATERIAL AND METHODS

Identification of cases

We performed a retrospective review of medical records of children 0–18 years old that presented to Umeå University hospital in Västerbotten county, Sweden, with an emergency reaction to food from January 1, 2006 to December 31, 2015. Patients treated by both paediatricians and emergency physicians at a secondary care level were included. Potential cases were identified by specific discharge codes according to the International Statistical Classification of Diseases, Tenth Revision (ICD-10) (Table 1). The medical records of the identified cases were manually reviewed by the same investigator (JÖ) to assess whether it was an emergency food reaction. A random sample of 120 cases presenting with asthma, ICD-10 code J45, were reviewed by an experienced paediatric allergist (CEW) to see if the group contained any cases with airway symptoms due to food reactions. No such cases were found, and this group was not reviewed further. The study was approved by the regional Ethical Review Board, Umeå, Sweden.

Data collection

Data were retrieved from the included cases and a standardised protocol was completed. The variables that were registered were age, sex, municipality of residence, symptoms grouped according to the affected organ system, food triggers, drug therapy and the level of care. Unclear cases and ambiguities were discussed with the paediatric allergist (CEW). A reaction was considered to be food triggered if the patient presented with typical symptoms of an allergic reaction following exposure to a suspected food

trigger. Serum immunoglobulin E (IgE) levels and a skin prick test for the suspected food triggering the allergic reaction were also reviewed, when available, but were not mandatory for diagnosis (14). Patients with repeated reactions to the same food trigger, but on different occasions, were included as a new event. Airway and cardiovascular symptoms were registered if they were objectively observed by a healthcare professional or reported by an adult witness. The other symptom categories were registered on the basis of objective findings and patient or parent-reported symptoms. No distinction between upper and lower airway symptoms was made, due to difficulties distinguishing them retrospectively based on medical records. Data on vital signs were not registered in detail but were assessed when they were available.

The triggering food allergens were registered in as much detail as possible. For the statistical analysis, milk, eggs, wheat, soy and fish were grouped together as staple foods. Triggering food was registered as unidentified if a single trigger could not be identified in the medical record. All drug therapy given after the onset of symptoms were registered, including drugs administered at home, in the ambulance and at the hospital.

Diagnosis of anaphylaxis

Anaphylaxis was retrospectively diagnosed by the use of criteria presented in the summary report of the Second symposium on the definition and management of anaphylaxis (10). These criteria state that anaphylaxis is highly likely when the patient presents with symptoms from at least two of the following organ systems, with a rapid onset after exposure to a likely allergen: skin and mucous membrane, respiratory, cardiovascular or digestive system. Anaphylaxis is also highly likely when a patient with a known allergy presents with hypotension following exposure to a previously known allergen. Patients with suspected food protein-induced enterocolitis syndrome (FPIES), a type of non-IgE mediated allergy (15), were separated from the anaphylaxis group, even if they met the criteria for anaphylaxis, as FPIES is a separate entity.

Statistical handling of data

Differences in proportions between the groups were analysed with the chi-square test and Fisher's exact test when applicable. The incidence trend was calculated with the Spearman's rank correlation test (r_s). Cases that did not belong to the catchment area of Umeå University hospital were excluded in the calculation of incidence trends. Population data were provided by Statistics Sweden (16). SPSS version 24.0 (IBM Corp, New York, USA) was used for the statistical analyses. A p value of <0.05 was considered significant.

RESULTS

Study population

We manually reviewed 1591 emergency medical records, which yielded 519 cases of allergic food reactions (58%

Table 1 Discharge codes for identification of potential cases according to the International Classification of Disease, Tenth Revision (ICD-10)

Code	Diagnosis
J45	Asthma
K52.2	Allergic and dietetic gastroenteritis and colitis
L20	Atopic dermatitis
L27	Dermatitis due to substances taken internally
L50.0	Allergic urticaria
L50.9	Urticaria, unspecified
T78.0	Anaphylactic shock due to adverse food reaction
T78.1	Other adverse food reactions, not elsewhere classified
T78.2	Anaphylactic shock, unspecified
T78.3	Angioneurotic oedema
T78.4	Allergy, unspecified
T78.8	Other adverse effect, unspecified
T78.9	Adverse effect, unspecified

boys). Of these, 99 reactions were classified as anaphylaxis and 29 as suspected FPIES (Fig. 1). Patients from outside the Umeå University hospital catchment area accounted for 36 cases, including 12 that were classified as anaphylaxis. The median (25th–75th percentile) age was 1.3 (0.4–7.8) years and it was 1.2 (0.4–4.8) years in boys and 1.3 (0.4–12.1) years in girls. The median age when the patients reacted to staple foods was 0.5 (0.3–1.2) years, compared to 5.6 (2.3–12.5) years in patients reacting to peanuts and tree nuts and 10.8 (2.7–16.8) years in those reacting to fruits and vegetables (Fig. 2).

Trigger foods

Milk caused 170 of the 519 reactions (32%), peanuts and tree nuts 115 reactions (22%), eggs 79 reactions (14%) and unidentified foods 103 reactions (20%). Peanuts was the most common single food to cause anaphylaxis (21%) followed by unidentified foods (16%) and eggs (14%). Tree nuts and almonds as a group accounted for 22% of the anaphylactic reactions, with cashew nuts (8%) and hazelnuts (7%) being the most common food triggers within the group. The distribution of all food triggers is displayed in Table 2.

Symptom presentation

Skin symptoms were the most frequently occurring symptom (70%), followed by gastrointestinal symptoms (43%) and oral symptoms (29%). The two trigger groups, fruits and vegetables and peanuts and tree nuts, caused oral symptoms in more than 50% of the cases, with a p value of <0.05 when they were compared with staple foods and unidentified foods. Reactions to peanuts and tree nuts involved airway symptoms in 31% of the cases, with a p value of <0.05 compared with staple foods and fruit and vegetables. Staple

foods elicited gastrointestinal symptoms in 50% of the, with a p value of <0.05 compared with fruits and vegetables and unidentified foods. The distribution of all symptoms is displayed in Table 3.

Clinical management

A total of 168 reactions (32%) led to hospitalisation and 71 (42%) of these were classified as anaphylaxis. Only one child (0.2%) needed intensive care. Adrenaline was administered in 74 (75%) of the 99 cases of anaphylaxis and 52 (70%) of these patients received it first at the hospital. In 33 (6%) of the 519 cases, the child had been injected with adrenaline at home and 20 (61%) of these 33 reactions were not classified as anaphylaxis. Bronchodilators were given in 33 (33%) of the 99 cases with anaphylaxis. Adrenaline auto-injector devices were prescribed, or had previously been prescribed, in 78 (79%) of the cases with anaphylaxis.

Incidence of anaphylaxis

The number of children aged 0–18 years living in the municipalities of Umeå, Vännäs, Nordmaling, Bjurholm, Vindeln and Robertsfors during the study period constituted a total of 289 977 person-years (16). Thus, the incidence of food triggered anaphylaxis during the 10-year period was 30 per 100 000 person-years.

Incidence trends

The incidence trend over this 10-year period was analysed for allergic reactions to the four large groups of food triggers: staple foods, peanuts and tree nuts, fruits and vegetables and unidentified foods (Fig. 3). The incidence trend of allergic reactions to eggs showed a positive correlation ($r_s = 0.770$, $p < 0.01$). No significant correlation was found in separate analyses for allergic reactions to milk,

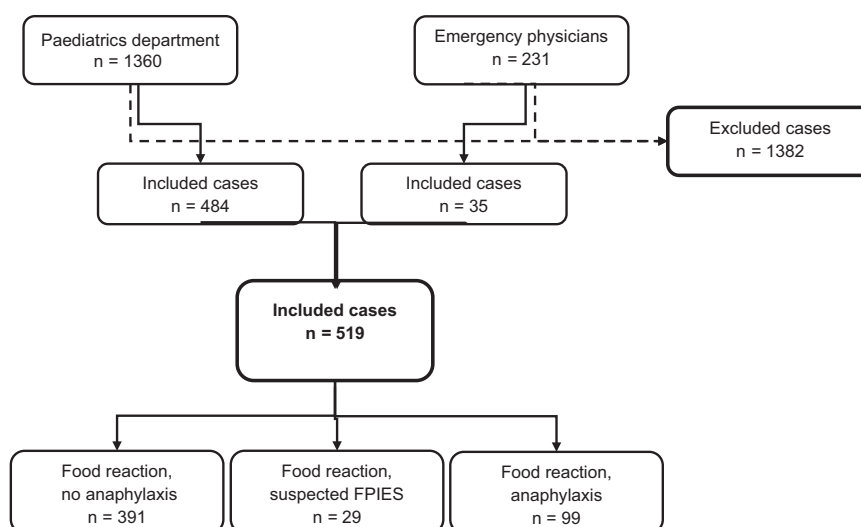


Figure 1 Schematic view of the review process of medical records and inclusion of patients seeking emergency care at Umeå University hospital between 2006 and 2015.

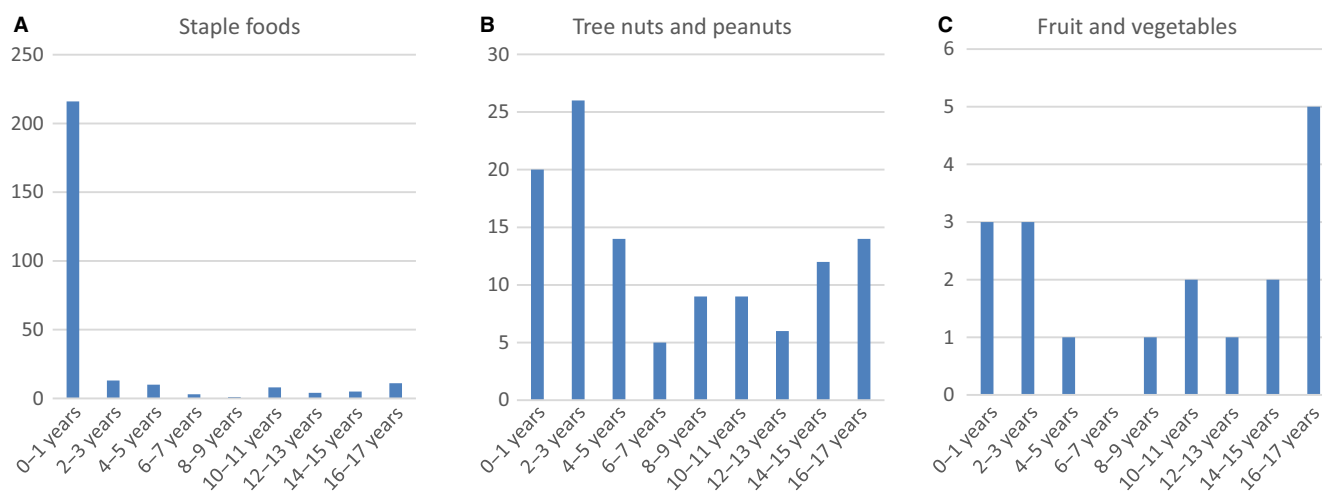


Figure 2 Age distribution for the number of reactions to staple foods (A), tree nuts and peanuts (B) and fruits and vegetables (C).

peanuts, hazelnuts and cashew nuts. An increasing incidence trend of food-induced anaphylaxis during the study period was also found ($r_s = 0.745$, $p = 0.013$).

DISCUSSION

In this retrospective study, we examined all children and adolescents admitted to Umeå University hospital for emergency food allergy reactions during a 10-year period. We found an increasing incidence of food-induced anaphylaxis and allergic reactions to eggs. The increase in food-induced anaphylaxis has not been previously described in a Swedish study. However, it is consistent with the increasing incidence trends of food allergies and anaphylaxis described in international studies (1) and increasing trends of hospitalisation, including anaphylaxis, due to allergic reactions in Sweden (17). Consequently, this calls for validation in prospective studies.

The incidence of food-triggered anaphylaxis during the 10-year period was 30 per 100 000 person-years, which was similar to the previously reported incidence of 29 anaphylactic reactions per 100 000 person-years in a retrospective study in Stockholm, Sweden (9). We used the international criteria for anaphylaxis proposed by Sampson et al. (10) in all cases, to acquire a more homogenous group of patients than we would have done if we had used the attending physicians' interpretations of the reaction severity.

Milk, eggs, peanuts and tree nuts, together with unidentified foods, were the most common triggers of allergic food reactions and anaphylaxis in this study population, which was in line with previous studies (1,2,8,9). Allergic reactions to staple foods, including milk and eggs, occurred mostly during the first two years of life unlike allergic reactions to peanuts, tree nuts, fruits and vegetables, which showed a more even distribution across all ages. This follows the common pattern of how foods are introduced into the children's diet and could also reflect the development of a natural tolerance to milk and eggs (7,18–20). To enable us to

compare emergency food reactions and anaphylaxis between the populations in northern and southern Sweden, we used a quite similar study design to two previous Swedish studies (8,9). In our setting, the median age of patients was 1.3 years, which was lower than the reported median age of 4.0 and 5.9 years in those studies (8,9). Patients who reacted to staple foods had the lowest median age, namely six months. A possible explanation for the high incidence of infants with emergency food allergic reactions in our study, compared to the studies in southern Sweden, could be the structure of paediatric healthcare in Sweden. Primary care paediatricians are rare in Västerbotten county, where our study took place, whereas they are common in primary care settings in southern Sweden. Consequently, parents in Västerbotten county may have been more likely to seek secondary care for mild to moderate allergic reactions in their infants. Symptoms relating to the skin and gastrointestinal system were the most common ones. The high incidence of gastrointestinal symptoms compared to other studies (8,9) is probably also an expression of the high prevalence of infants presenting with reactions to staple foods.

Cases classified as anaphylaxis received adrenaline injections in 75% of the cases. In a 2018 report from the European Anaphylaxis register (21), only a small proportion of anaphylaxis incidents were treated with adrenaline despite clear guidelines, underscoring the need for greater educational and physician training programmes. In Sweden, the national recommendations on anaphylaxis treatment were updated in 2015, including the paediatric dosages of adrenaline (22). As far as we know, adrenaline auto-injector devices were prescribed for 79% of the 99 children with anaphylaxis in our study, but this could have been an underestimation, since we lacked information from patients followed up in primary care and from patients that resided in other counties. However, this figure could be consistent with the recommendations by the Swedish Association for Allergy, which states that it is mandatory to prescribe adrenaline auto-injector devices for grade 2–3 anaphylaxis

Table 2 Trigger foods in 519 cases of emergency food reactions in children and adolescents that presented at Umeå University hospital during a 10-year period from January 1, 2006 to December 31, 2015

	Allergic reaction No anaphylaxis n = 420 A n (%)	Allergic reaction Anaphylaxis n = 99 B n (%)	p values A vs B
Milk n = 170 (33%)	157 (37)	13 (13)	<0.001
Egg n = 79 (15%)	65 (15)	14 (14)	0.74
Tree nuts and almonds n = 71 (14%)	49 (12)	22 (22)	<0.01
Hazelnuts n = 24 (5%)	17 (4)	7 (7)	0.20
Cashew nuts n = 19 (4%)	11 (3)	8 (8)	<0.01
Nuts unspecified n = 13 (3%)	9 (2)	4 (4)	0.28
Walnuts n = 8 (2%)	4 (1)	4 (4)	<0.05
Brazil nut n = 3 (0.6%)	2 (0.5)	1 (1)	0.53
Pistachio n = 2 (0.4%)	1 (0.2)	1 (1)	0.26
Almond n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Peanuts n = 46 (9%)	25 (6)	21 (21)	<0.001
Fish n = 15 (3%)	12 (3)	3 (3)	0.93
Salmon n = 5 (1%)	5 (1)	0 (0)	0.28
Unspecified n = 6 (1%)	5 (1)	1 (1)	0.88
Others n = 3 (0.6%)	1 (0.2)	2 (2)	<0.05
White fish n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Fruits n = 13 (3%)	11 (3)	2 (3)	0.73
Kiwi n = 2 (0.4%)	1 (0.2)	1 (2)	0.26
Citrus n = 3 (0.6%)	3 (0.7)	0 (0)	0.84
Mango n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Apple n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Peach n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Cherry n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Pomegranate n = 1 (0.2%)	0 (0)	1 (1)	<0.05
Strawberry n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Pear n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Vegetables n = 5 (1%)	3 (0.7)	2 (2)	0.23
Chickpeas n = 2 (0.4%)	0 (0)	2 (2)	<0.01
Peas n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Tomato n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Avocado n = 1 (0.2%)	1 (0.2)	0 (0)	0.62
Soy n = 5 (1%)	3 (0.7)	2 (2)	0.23
Wheat n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Shellfish n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Shrimp n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Other n = 4 (0.8%)	4 (0.9)	0 (0)	0.33
Oat n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Mustard seeds n = 2 (0.4%)	2 (0.5)	0 (0)	0.49
Unidentified n = 103 (20%)	87 (21)	16 (16)	0.31

Bold font indicates a statistically significant difference $p < 0.05$.

Table 3 Distribution of symptoms in relation to the triggering food

Symptoms	Staple foods n = 271 n (%)	Fruits and vegetables n = 18 n (%)	Peanuts and tree nuts n = 115 n (%)	Unidentified n = 103 n (%)
Skin n = 364 (70%)	175 (65)	11 (61)	88 (77)	82 (80)
Oral n = 152 (29%)	41 (15)	11 (61)*	63 (55)*	33 (32)
GI n = 224 (43%)	136 (50)**	2 (11)	49 (43)	30 (29)
Airway n = 85 (16%)	24 (9)	3 (17)	36 (31)***	18 (17)
Cardiovascular n = 15 (3%)	8 (3)	1 (6)	2 (2)	3 (3)
Neurological n = 2 (0.4%)	1 (0.4)	0 (0)	0 (0)	1 (1)

* $p < 0.05$ compared with reactions to staple foods and unidentified foods.

** $p < 0.05$ compared with reactions to fruits and vegetables and unidentified foods.

*** $p < 0.05$ compared with reactions to staple foods and fruit and vegetables.

adrenaline was administered at home (61%) did not meet the criteria for anaphylaxis, but it is likely that these cases could have progressed to anaphylaxis. This could have led to an underestimation of the incidence of anaphylaxis in this study. Detailed data on vital signs were not available from all the medical records, which is another limitation. The possibility of misclassification or even neglecting symptoms is a known limitation of this type of study. Identifying cases using diagnostic codes also has its limitations when establishing the incidence at a population level, since the diagnostic codes describe the symptoms of allergies rather than the prevalence. Thus, large prospective epidemiological studies are required to describe the true incidence and incidence trend of food-induced anaphylaxis at a population level. We studied patients who presented with emergency food reactions at the hospital, who represented a secondary care level, and therefore we can assume that some children with milder emergency food reactions were treated in primary care settings. However, as Umeå University hospital has the only paediatric department in the region, we can assume that all patients with severe reactions presented directly to the hospital or were referred from primary care.

A major strength of our study is the use of a large number of diagnostic codes, both codes that are specific for food allergies as well as broader allergy codes. This ensured that we identified the majority of the food reactions during the period, even if they were incorrectly coded within the group of diagnostic codes associated with allergic diseases. Out of the 1591 emergency visits, 519 cases of food reactions were identified, which illustrates the problem of incorrectly coded or incomplete medical records. The study period of 10 years enabled us to present a more accurate analysis of time trends. We also had access to the complete paediatric medical record of patients, which enabled us to follow the

patients, but that the indication for prescribing adrenaline is relative in patients with grade 1 anaphylaxis (22).

The main limitation of this study is its retrospective approach, which warrants caution when interpreting the study findings. Thorough documentation of the event in the medical records is required by the attending physician for a correct classification. A high proportion of the cases where

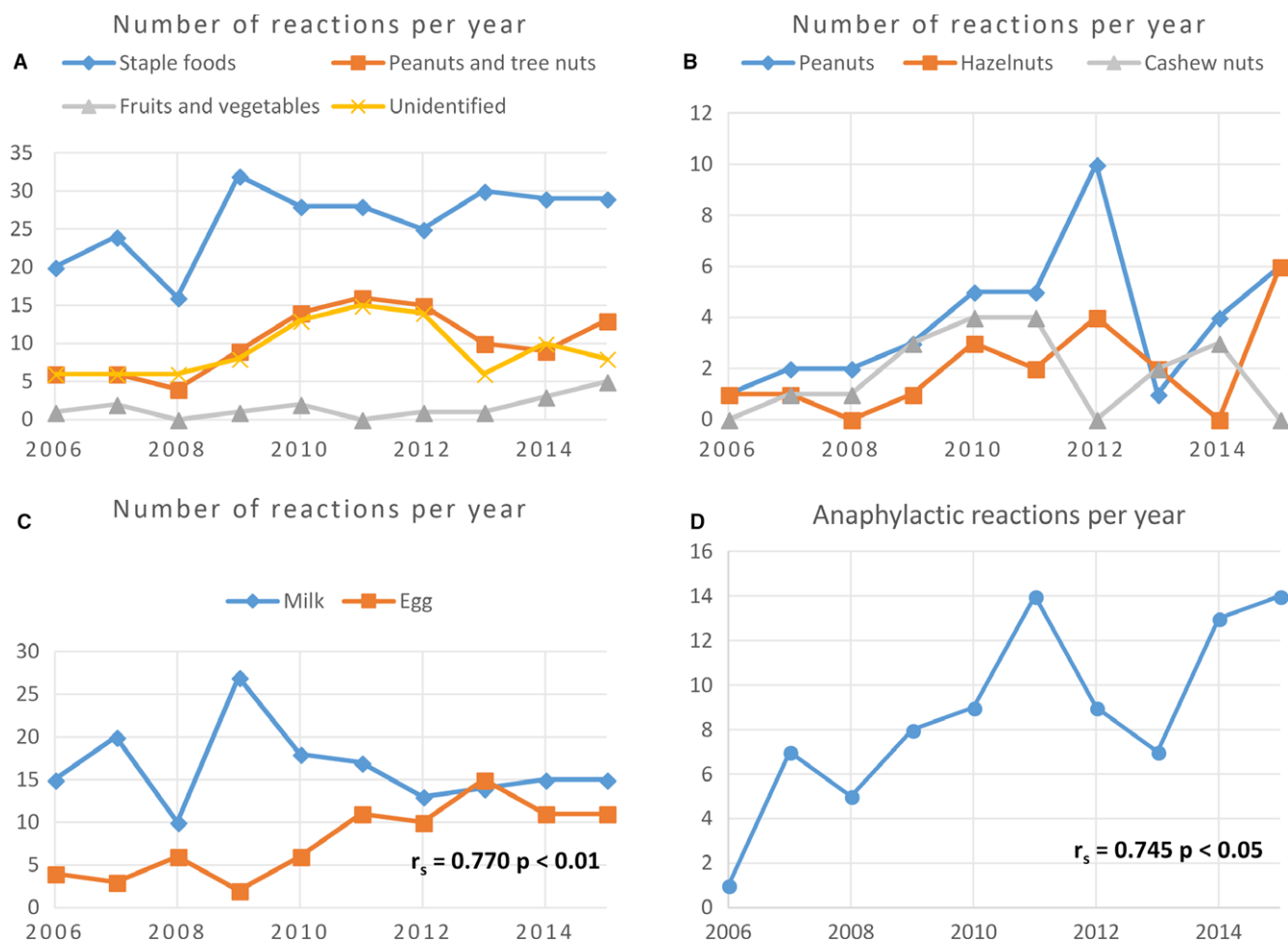


Figure 3 The total number of allergic reactions per year (2006–2015) in patients living in the municipalities of Umeå, Vännäs, Nordmaling, Bjurholm, Vindeln and Robertsfors. Reactions to staple foods, peanuts and tree nuts, fruits and vegetables and unidentified foods (A) and reactions to cashew nuts, hazelnuts and peanuts (B) and milk and eggs (C). Number of anaphylactic reactions due to food per year during 2006 to 2015 (D).

diagnostic process to find the trigger foods more precisely with the help of IgE levels and skin prick tests, when available.

CONCLUSION

We found that emergency egg allergy reactions and food-induced anaphylaxis increased in children from 2006 to 2015 at a secondary care level in northern Sweden. These findings call for large prospective epidemiological studies to describe the true incidence and incidence trend of food allergies and food-induced anaphylaxis.

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CONFLICT OF INTEREST

The authors have no conflicts of interests to declare.

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