

Recurrent reactions to food among children at paediatric emergency departments

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Summary

Background Knowledge about repeated food reactions in paediatric emergency departments (ED) is sparse.

Objective To investigate the incidence and potential risk factors for repeated ED visits for food-allergic reactions among children with a prior ED visit due to reactions to food.

Methods A total of 358 children with ED visits at paediatric hospitals in Stockholm due to reactions to foods during 2007 (index-reaction) were investigated in relation to recurrent reactions until 30 June 2010. Adjusted Cox proportional hazard models were used to compute relative risks (RR) and 95% confidence intervals (CI).

Results A total of 80 children had 116 ED revisits over a period of 873 patient-years, yielding an incidence rate of 9 per 100 patient-years. Known food allergy before the index ED visit in 2007 increased the risk for ED revisits (RR = 2.30, 95% CI 1.35–3.94). Likewise, prescription of adrenaline auto-injector before the index-reaction increased the risk (RR = 2.02, 95% CI 1.17–3.49). Twenty-one percent of the children had more severe reactions at the revisit, 38% less severe and 41% had reactions of comparable severity. However, among 44% of the children with comparable or less severe reaction at revisit, early treatment with adrenaline hampered the classification of change in severity.

Conclusions and Clinical Relevance Previously known food allergy and prior prescription of adrenaline are significant risk factors for ED revisits among children with a prior ED visit due to reactions to food. Our results indicate that the severity of the index-reaction cannot be used to predict the severity of the relapse.

Keywords anaphylaxis, children, emergency department, food allergy

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Introduction

Food allergy represents a major health issue, and it has to date not been possible to predict the severity of future reactions on an individual basis [1]. Therefore, the fear of a future fatal reaction can be a source of considerable anxiety in families of food-allergic children [2]. As there is no established curative treatment of food allergy, management relies on careful diagnostic procedures, followed by avoidance and at accidental exposure to a culprit allergen, early recognitions of symptoms followed by pharmacological treatment. However, as efficient avoidance may be difficult, the risk of further accidental exposure is not negligible. Thus, there is a need of agreement of which patients are at risk of anaphylaxis [3].

Knowledge about accidental allergic reactions in the paediatric population is scarce with previous studies focusing on single foods and nuts [4–7]. Few studies have evaluated risk factors for accidental allergic reactions among children and the risk of a more severe reaction at re-exposure [6–9]. To our knowledge, no study on accidental allergic reactions has been performed in a paediatric emergency department (ED) setting.

The objectives of this study were to determine the incidence of ED revisits due to allergic reactions to foods in a cohort of 358 children. Furthermore, to investigate potential risk factors for ED revisits and to determine the risk of impairment at rereactions in this group of children.

Materials and methods

Study population

In a review of medical records, all 371 children with ED visits due to allergic reactions to foods at all the three paediatric hospitals in Stockholm County during 2007 could be identified, which has been described elsewhere [10].

In this study, we reinvestigated the study population in relation to new ED visits due to reactions to foods. Children not resident in Stockholm County at the index-reaction were excluded as they were unlikely to visit any of the paediatric EDs in Stockholm in case of a new allergic reaction to foods, leaving 358 children for inclusion in the cohort (Fig. 1). The follow-up period was between 1 January 2007 and 30 June 2010.

Identification of ED revisits

Medical records of all 358 children were reviewed to identify any visits to the ED departments during the time of follow-up. Two new local emergency units affiliated to two of the paediatric hospitals opened during the follow-up period. The medical records at these units were reviewed as children with milder reactions to food could have been admitted there when they visited the ED department.

The 358 medical records were reviewed, and information regarding all ED revisits due to allergic reactions to foods was recorded with the same procedure described previously [10]. Data on current allergic diseases, probable eliciting foods, pharmacological

treatment including self-injectable adrenaline and referral for follow-up were also collected. Furthermore, we retrieved complete data of medical records of each patient including inpatient and outpatient visits prior to, but also after the ED revisit. The eliciting food was recorded as 'unknown' if no single food could be identified or when more than one trigger was suggested. Clinical data were extracted using a predefined protocol.

Classification of reactions

We used the criteria for anaphylaxis and the severity grading from the EAACI Task Force Anaphylaxis paper by Muraro et al. [11], although slightly modified by us [12]. The children were allocated into four groups [10, 12]: 1 – No anaphylaxis, no adrenalin given, 2 – no anaphylaxis, adrenalin given, 3 – Anaphylaxis – mild–moderate, 4 – Anaphylaxis – severe.

Statistical analysis

Means, range and standard deviation were compiled for the continuous variable age. Incidence and prevalence were calculated. The incidence rate of ED revisits was computed as the number of events divided by the sum of the patient-years at risk and expressed as the rate of ED revisits per 100 patient-years. Prevalence rates are presented as percentages. Nominal data were compared by the chi-square test. The independent t-test was used to compare means. A value of $P < 0.05$ was considered as significant.

We computed person-time of follow-up for each child from the date of the index-reaction in 2007 to the date of the first ED revisit, date of 18 years birthday, date for moving away from Stockholm county or end of follow-up (June 30, 2010), whichever occurred first. The continuously updated Swedish National Population Register allowed us to identify when a child had moved out of the catchment area/Stockholm County. Cox proportional hazards regression was used to estimate relative risks (RRs) and the corresponding 95% confidence intervals (CIs) for possible risk factors for ED revisits. To examine the proportionality assumption, cumulative hazard functions for all covariates were plotted.

Patient characteristics evaluated as possible risk factors for ED revisits included sex, age group, hospital of initial recruitment, visit season, severity of the index-reaction, eliciting foods at the index-reaction, history of the following atopic diseases prior to the index-reaction: food allergy, asthma, eczema, allergy to inhalant allergens and prescription of adrenaline auto-injector before the index-reaction. The same covariates were assessed for the possibility of confounding and

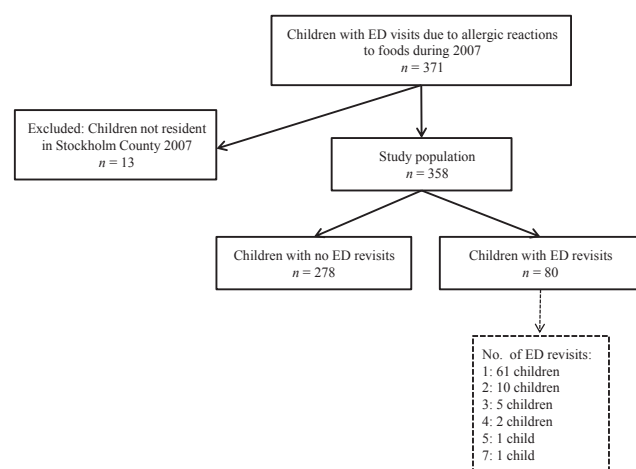


Fig. 1. Description of the cohort of children with index ED visits during 2007 due to allergic reactions to foods and final allocation into two groups: children with ED revisits versus children with no ED revisits due to allergic reactions to foods during follow-up (1 January 2007–30 June 2010).

included in the final model if they changed the estimate of the crude RRs by more than 10%. These factors were age, eliciting food, food allergy, asthma, allergy to inhalant allergens and prescription of adrenaline. However, as food allergy is highly correlated with asthma, allergy to inhalant allergens and prescription of adrenaline, we decided to not include the latter three covariates in the final multivariable model. Sex had small confounding effects but was kept in the final multivariable model.

All statistical analyses were carried out with the statistical program SPSS 20 (SPSS, Inc, Chicago, USA III).

The study was approved by the Regional Ethical Review Board, Stockholm, Sweden.

Results

Rate of ED revisits and patient characteristics

During the study period, 80 children of 358 (22%) had a total of 116 ED revisits due to reactions to foods over a period of 873 patient-years. This yields an incidence rate of ED revisits of 9 per 100 patient-years. A total of 19 children had more than one ED revisit during follow-up (Fig. 1).

In Table 1, characteristics of children with no ED revisits ($n = 278$) and children with ED revisits during follow-up are presented. At the time for the index-reaction, the two groups were similar in terms of proportion of girls, age, severity of the reaction and eliciting foods. ED revisits were statistically significantly more common among children with a diagnosis of food allergy and prescription of adrenaline auto-injector (AAI) before the index-reaction.

Eliciting foods and symptoms at the ED revisit

Eliciting foods and severity of the reactions at the ED revisit are reported in Table 1. For 20% of children with anaphylaxis at the ED revisit, the eliciting food was unknown. In comparison with the index-reaction, 19 (24%) reacted to the same food and 14 (18%) to a different food (data not shown). In 47 children (59%), it remained unclear whether they had reacted to the same or a different food as the eliciting food was unknown at either the index-reaction or at the ED revisit. The proportion of children in which the eliciting food was unknown was not significantly higher among children not referred for follow-up compared with those referred for follow-up after the index-reaction in 2007 (data not shown).

No child suffered respiratory arrest or fatal course at the ED revisits. However, one child was unconscious, one had hypotension, and another child was admitted to intensive care.

Table 1. Characteristics of the study population of 358 children admitted to paediatric emergency departments in Stockholm, Sweden, in 2007 for allergic reactions to foods, followed for potential revisits until June 2010

	Children with no ED revisits $n = 278$	Children with ED revisits $n = 80$	Reaction at ED revisit
	Index- reaction	Index- reaction	
Person-years, n	783	90	
Age in years			
Mean (SD)	5.7 (5.5)	5.0 (4.6)	6.1 (4.9)
Range	0, 17	0, 16	0, 17
Sex – girls, n (%)	129 (46)	40 (50)	
Allergic disease comorbidity,			
Previously known	154 (55)	58 (73)	74 (93)
food allergy,* n (%)			
1 food allergy,	79 (28)	24 (30)	25 (31)
n (%)			
2 $\geq$ food allergies,	75 (27)	34 (43)	49 (61)
n (%)			
Asthma, n (%)	79 (28)	27 (34)	37 (46)
Eczema, n (%)	68 (25)	24 (30)	33 (41)
Allergy to inhalant	77 (28)	27 (34)	36 (45)
allergens, n (%)			
Adrenaline auto-	48 (17)	26 (33)	57 (71)
injector prescribed			
before ED			
visit*, n (%)			
Severity of reaction,			
No anaphylaxis, no	135 (49)	32 (40)	33 (41)
adrenaline given,			
n (%)			
No anaphylaxis,	52 (19)	15 (19)	27 (34)
adrenaline given,			
n (%)			
Anaphylaxis, mild-	79 (28)	27 (34)	16 (20)
moderate, n (%)			
Anaphylaxis, severe,	12 (4)	6 (8)	4 (5)
n (%)			
Eliciting foods,			
Any tree nut-	113 (41)	25 (31)	28 (35)
peanuts, n (%)			
Egg, n (%)	32 (12)	10 (13)	10 (13)
Milk, n (%)	22 (8)	10 (13)	10 (13)
Other foods, n (%)	42 (15)	10 (13)	15 (19)
Unknown, n (%)	69 (25)	25 (31)	17 (21)
Referred for	204 (73)	54 (68)	37 (46)
follow-up, n (%)			

* P -value < 0.05 . Children with ED revisits compared with children with no ED revisits.

Risk factors for ED revisits

Relative risks (RR) and 95% confidence intervals (95% CI) for possible risk factors for ED revisits are presented in Tables 2 and 3. Known food allergy before the

Table 2. Relative risk and 95% CI of ED revisit in relation to various background factors and severity of reaction at the time point for the index ED visit in 2007

		Children with no ED revisits, <i>n</i> 278 (<i>n</i>)	Children with ED revisits, <i>n</i> 80 (<i>n</i>)	Age and sex adjusted model		Multivariable model	
				RR	95% CI	RR	95% CI
Age	0–2	120	34	1.0		1.0	
	3–6	47	20	1.41	0.81–2.45	1.04	0.57–1.90
	7–12	64	18	0.95	0.53–1.68	0.73	0.38–1.41
	13–17	47	8	0.73	0.34–1.59	0.56	0.24–1.30
Sex	Girls	129	40	1.0		1.0	
	Boys	149	40	0.84	0.54–1.31	0.84	0.54–1.31
Allergic disease							
comorbidity,							
Known food allergy	No	124	22	1.0		1.0	
	Yes	154	58	2.35	1.38–4.01	2.30	1.35–3.94
	1 food allergy	79	24	1.90	1.03–3.50	1.87	1.01–3.46
	2 ≥ food allergies	75	34	2.87	1.60–5.12	2.79	1.56–5.00
Asthma	No	199	53	1.0		1.0	
	Yes	79	27	1.32	0.80–2.19	1.09	0.66–1.81
Eczema	No	210	56	1.0		1.0	
	Yes	68	24	1.25	0.77–2.01	1.05	0.64–1.74
Allergy to inhalant allergens	No	201	53	1.0		1.0	
	Yes	77	27	1.72	0.97–3.04	1.73	0.97–3.10
Adrenaline auto-injector prescribed before ED visit	No	230	54	1.0		1.0	
	Yes	48	26	2.66	1.57–4.51	2.02	1.17–3.49
Severity of reaction in 2007	No anaphylaxis,	135	32	1.0		1.0	
	no adrenalin given						
	No anaphylaxis,	52	15	1.31	0.70–2.46	1.25	0.66–2.36
	adrenalin given						
	Anaphylaxis,	79	27	1.45	0.86–2.44	1.38	0.82–2.35
	mild–moderate						
	Anaphylaxis, severe	12	6	1.91	0.79–4.61	1.60	0.66–3.88

Multivariable model: adjusted for age, sex, eliciting food at reaction in 2007, known food allergy before the index-reaction in 2007.

Table 3. Relative risk and 95% CI of ED revisit according to eliciting food at the time point for the index-reaction in 2007

				Age and sex adjusted model				Multivariable model	
				RR	95% CI	RR	95% CI		
Specified foods									
Any tree nut- peanuts*	No	96	30	1.0		1.0			
	Yes	113	25	0.76	0.44–1.32	0.85	0.48–1.48		
Egg*	No	177	45	1.0		1.0			
	Yes	32	10	1.16	0.58–2.34	1.04	0.51–2.10		
Milk*	No	187	45	1.0		1.0			
	Yes	22	10	1.65	0.80–3.39	1.54	0.75–3.16		
Other foods*	No	167	45	1.0		1.0			
	Yes	42	10	0.90	0.45–1.80	0.88	0.44–1.75		
Eliciting food unknown	No	209	55	1.0		1.0			
	Yes	69	25	1.30	0.80–2.10	1.33	0.82–2.15		

Multivariable model: adjusted for age, sex, known food allergy before the index-reaction in 2007.

*Numbers do not sum to 358 (278 + 80) as children with reactions to unknown foods (*n* = 94) are not included.

index-visit in 2007 was identified as a risk factor for ED revisits (RR = 2.30, 95% CI 1.35–3.94) with a tendency towards higher risk among children with two or

more food allergies. Prescription of AAI before the index-reaction also emerged as a risk factor for ED revisits (RR = 2.02, 95% CI 1.17–3.49). Additional

adjustment for asthma and allergy to inhalant allergens did not change the results. Allergy to inhalant allergens before the index-reaction showed a tendency towards increased risk of ED revisits (RR = 1.73, 95% CI 0.97–3.10). Having a more severe index-reaction seemed to be positively associated with the risk for ED revisits, however, without reaching statistical significance most likely due to limited number of observations.

Severity of index-reaction compared with reaction at the ED revisit

Compared with the index-reaction, 21% were having a more severe reaction at the ED revisit, 38% a less severe reaction and the remaining 41% a reaction of comparable severity (Table 4). However, among 28 (44%) of the 63 children with comparable or less severe reaction at revisit, treatment with adrenaline, either at the index-reaction or at the ED revisits, hampered the classification of change in severity (Fig. 2). Among the 20 children with anaphylaxis at the ED revisit, treatment with adrenaline possibly influenced the change in severity in 11 (55%) of the children. Three children (4%) were classified as having a mild reaction (no anaphylaxis, no adrenalin given) at the index-reaction, but as having a severe anaphylaxis at the ED revisit (data not shown).

Compliance with adrenaline auto-injectors

Among the 80 children with ED revisits, 57 (71%) had been prescribed an AAI before the ED revisit. Twenty-three (40%) of these children had used their AAI at the time point for the ED revisit. Nineteen of the 23 children who had used their AAI did not fulfil the criteria for anaphylaxis at the ED revisit. Among some of these children,

early treatment with adrenaline might have prevented anaphylaxis. Among the 17 children who did fulfil the criteria for anaphylaxis at the ED revisit and had been prescribed an AAI, only four had used the device.

Children with multiple ED revisits

During follow-up, nine children had three or more ED revisits of which six (67%) had known allergy to egg or milk at the index-reaction. These six egg- or milk-allergic children had a total of 26 ED revisits. The eliciting food was egg or milk at ten of the 26 ED revisits, other specified foods at seven of the ED revisits and unknown at nine of the ED revisits.

Of the nine children with three or more ED revisits, seven were referred for follow-up already after the index-reaction. At the time point for their second ED

Table 4. Severity of the reaction at the ED revisit compared with the index-reaction among 80 children with repeated ED visits due to allergic reactions to foods

	Severity at ED revisit		
	Less severe reaction	Comparable severity	More severe reaction
Severity of the index-reaction			
No anaphylaxis, no adrenaline given, <i>n</i> (%)	n.a.	16 (50)	16 (50)
No anaphylaxis, adrenaline given, <i>n</i> (%)	6 (40)	8 (53)	1 (7)
Anaphylaxis, mild-moderate, <i>n</i> (%)	18 (67)	9 (33)	0 (0)
Anaphylaxis, severe, <i>n</i> (%)	6 (100)	0 (0)	0 (0)
Total, <i>n</i> (%)	30 (38)	33 (41)	17 (21)

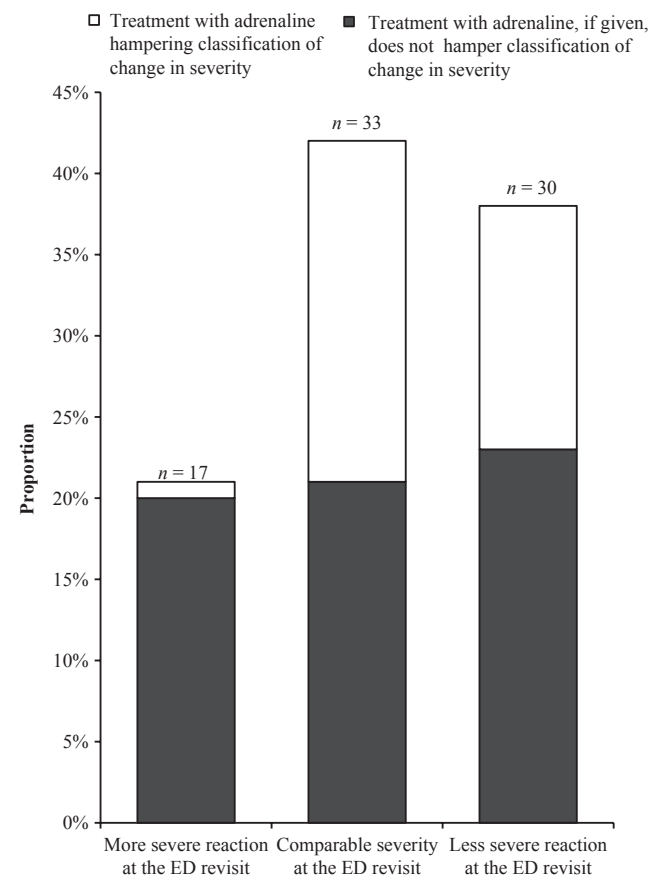


Fig. 2. Change in severity of the reactions among 80 children with repeated ED visits due to allergic reactions to foods. The total height of each bar represents the percentage of children in a given stratum of change in severity of the reaction, (ED revisit compared with the index-reaction). The white area of the bar represents the percentage of children in a given stratum of change in severity in which treatment with adrenaline, either at the index-reaction or at the ED revisits, could have influenced the severity of the reaction, thereby hampering classification of change in severity.

revisit, all nine children had an established contact with the healthcare system and the majority was treated by a paediatric allergy specialist.

Discussion

To our knowledge, this is the first study investigating the incidence rate, risk factors for accidental allergic reactions and change in severity over time due to reactions to foods in general and not only to a single food in a paediatric ED setting. Using longitudinal models, we could account for differences in time of exposure, for example, that patients contribute differently in relation to exposures and other factors as observational time is not equal.

Among children in our cohort, 22% had ED revisits due to reactions to foods during the follow-up period. This gives an incidence rate of ED revisits of 9 per 100 patient-years. This rate is lower than reported by others [4, 6]. For example, Fleischer et al. [9] reported an annualized incidence rate of allergic reactions to all foods of 81 per 100 patient-years among 512 preschool children with documented or likely allergy to milk and egg followed prospectively. However, direct comparisons are restricted by methodological differences between studies. In our study, we only captured allergic reactions presenting to a paediatric ED, while previous studies have examined the incidence of accidental allergic reactions in general. Comparisons are also limited by differences in healthcare system and access to health care.

The low incidence rate observed in our study may have several explanations besides the fact that we did not capture allergic reactions treated at home or at local healthcare providers. First, food allergies could have resolved from the time of the index-reaction in some of the patients. Secondly, we might have misclassified some children in our original study as having had reactions to food, but the original reaction was caused by another agent. Thirdly, the low incidence rate may be, at least partly, attributed to the fact that most children had medical follow-ups after the index-reaction. Adequate secondary preventive strategies after reactions to foods have previously been shown to reduce the risk of relapse [5].

In the present study, we identified two risk factors for ED revisits: food allergy before the index ED visit, with a more pronounced risk among children with two or more food allergies, and prescription of AAI before the index-reaction. In addition, allergy to inhalant allergens before the index-reaction was associated with a tendency towards an increased risk of ED revisits. All these three baseline factors could be seen as a proxy for more severe allergic disease, as well as markers for true food allergy. Hence, these findings are not surprising. That a greater number of food allergies were associated with having

accidental rereactions could be expected based on probability and has been shown by others [9, 13]. Cummings et al. [14] have showed that prescription of AAIs was associated with reduced anxiety for food-allergic children and their mothers, but not with improved adherence with medical management or reduced risk taking. They argue that the reduced anxiety may reduce families' vigilance. Hypothetically, this could partly explain our finding of prescription of AAI as a risk factor for ED revisits. Although previously known food allergy and prior prescription of adrenaline were identified as risk factors for ED revisits, the possibility to predict a future allergic reaction based on these factors is poor.

Having reactions elicited by tree nuts or peanuts at the index-reaction did not stand out as major risk factors for ED revisits compared with milk and egg. To us, this finding was unexpected as nut allergy is more likely to be lifelong compared with allergies to milk and egg. However, as milk and egg may be hidden in many products and lack strong smell and flavour compared with nuts, we speculate that accidental intake to food items such as milk and egg might be more likely compared with nuts. Our finding that the majority of children with multiple ED revisits were egg or milk allergic supports this reasoning. In addition, milk has been shown to cause high rates of accidental reactions among children with milk allergy [4, 9].

Besides previously known food allergy and prior prescription of adrenaline, no other risk factors for ED revisits were identified in our multivariable analyses, although a severe index-reaction has been suggested by others to increase the risk of recurrent reactions [6]. However, our non-significant associations should be interpreted by caution due to the relatively low number of children with ED revisits.

No specific eliciting food could be identified either at the index-reaction or at the ED revisit among 59% of the children. It could be speculated that the proportion of children in which the eliciting food remains unknown might be higher among those not being referred for follow-up after an ED visit compared with those being referred. However, this was not the case in our cohort.

The severity of the reaction at the ED revisit could not be accurately predicted by the severity of the index-reaction, which is in line with previous reports [5–7, 15]. Although 41% of the children had reactions of comparable severity, 38% had less severe reactions and 21% more severe reactions at the ED revisit. However, among 44% of the children with comparable or less severe reaction at revisit, treatment with adrenaline hampered the classification of change in severity. This risk of misclassification of change in severity due to early treatment with adrenalin has rarely been discussed in previous studies in this field. In the light of recent years of research of allergic reactions to food, including

our study, food allergy emerges as an unpredictable disease. In a recent study where 27 peanut-sensitized children underwent a double-blind placebo-controlled food challenge followed by a single-blind oral food challenge, the threshold dose and severity scoring were not reproducible [16]. Taken together, if these results and the results by us are true, this ought to have consequences for the management of food-allergic children.

Delay in the administration of adrenaline is a consistent risk factor for fatal food-induced anaphylaxis [17–20]. Hence, it is alarming that the vast majority of children with anaphylaxis prescribed with adrenaline in our study did not use their device. This finding is in line with others [9, 21, 22] and indicates a need for a change in attitudes of anaphylaxis self-management. On the other hand, in total, 40% of all children prescribed with AAI used their device which might have prevented some from having more severe reactions.

One limitation of this study is our reliance on documentation in the medical records at data collection as there is no guarantee that all symptoms and signs at reaction and underlying allergies have been asked for and included in the medical records. A major strength in this study is that we used Cox proportional hazards regression to estimate relative risks. Another strength is that we, unlike most earlier studies, tried to capture reactions to multiple foods. By doing this, we could show that reactions when eating full meals often hamper a final diagnosis of allergy to a certain food. Furthermore, even if data collection from medical records has its limitations due to limited information, the information which is there is highly reliable compared with parent's or children's retrospective recall of clinical features collected from questionnaires. Moreover, the information was recorded at the index-reaction, so any misclassification of symptoms and signs at reaction etc. is likely to be non-differential between children with and without ED revisits, leading only to underestimation of the true association.

In conclusion, this cohort study reports on the incidence and potential risk factors for repeated ED visits for food-allergic reactions among children with a prior ED visit due to reactions to food. The incidence of ED revisits for food-allergic reactions was 9 per 100 person-years. Previously known food allergy and prior prescription of

adrenaline were identified as significant risk factors for ED revisits. The severity of the reaction at the ED revisit could not be predicted by the severity of the index-reaction, and classification of change in severity was often hampered by early treatment with adrenaline. The vast majority of children with anaphylaxis at the ED revisit, previously prescribed with adrenaline, failed to use their device. This study adds to the current body of literature by investigating clinical relevant exposures for repeat ED visits due to food-allergic reactions using longitudinal models. Additionally, the study provides information about the unpredictability of the food-allergic condition as well as the difficulties associated with studying the disease.

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Conflict of interest

The authors declare that they have no conflict of interest.

References:

- 1 Burks AW, Tang M, Sicherer S *et al*. ICON: food allergy. *J Allergy Clin Immunol* 2012; 129:906–20.
- 2 Klennert MD, Robinson JL. Addressing the psychological needs of families of food-allergic children. *Curr Allergy Asthma Rep* 2008; 8:195–200.
- 3 Niggemann B, Beyer K. Adrenaline autoinjectors in food allergy: in for a cent, in for a euro? *Pediatr Allergy Immunol* 2012; 23:506–8.
- 4 Boyano-Martinez T, Garcia-Ara C, Pedrosa M, Diaz-Pena JM, Quirce S. Accidental allergic reactions in children allergic to cow's milk proteins. *J Allergy Clin Immunol* 2009; 123:883–8.
- 5 Clark AT, Ewan PW. Good prognosis, clinical features, and circumstances of

- peanut and tree nut reactions in children treated by a specialist allergy center. *J Allergy Clin Immunol* 2008; 122:286–9.
- 6 Nguyen-Luu NU, Ben-Shoshan M, Alizadehfar R *et al*. Inadvertent exposures in children with peanut allergy. *Pediatr Allergy Immunol* 2012; 23: 133–9.
 - 7 Vander Leek TK, Liu AH, Stefanski K, Blacker B, Bock SA. The natural history of peanut allergy in young children and its association with serum peanut-specific IgE. *J Pediatr* 2000; 137:749–55.
 - 8 Ewan PW, Clark AT. Efficacy of a management plan based on severity assessment in longitudinal and case-controlled studies of 747 children with nut allergy: proposal for good practice. *Clin Exp Allergy* 2005; 35:751–6.
 - 9 Fleischer DM, Perry TT, Atkins D *et al*. Allergic reactions to foods in pre-school-aged children in a prospective observational food allergy study. *Pediatrics* 2012; 130:e25–32.
 - 10 Vetander M, Helander D, Flodstrom C *et al*. Anaphylaxis and reactions to foods in children—a population-based case study of emergency department visits. *Clin Exp Allergy* 2012; 42:568–77.
 - 11 Muraro A, Roberts G, Clark A *et al*. The management of anaphylaxis in childhood: position paper of the European academy of allergology and clinical immunology. *Allergy* 2007; 62:857–71.
 - 12 Vetander M, Helander D, Lindquist C *et al*. Classification of anaphylaxis and utility of the EAACI Taskforce position paper on Anaphylaxis in Children. *Pediatr Allergy Immunol* 2011; 22:369–73.
 - 13 Kapoor S, Roberts G, Bynoe Y, Goughan M, Habibi P, Lack G. Influence of a multidisciplinary paediatric allergy clinic on parental knowledge and rate of subsequent allergic reactions. *Allergy* 2004; 59:185–91.
 - 14 Cummings AJ, Knibb RC, Erlewyn-Lajeunesse M, King RM, Roberts G, Lucas JS. Management of nut allergy influences quality of life and anxiety in children and their mothers. *Pediatr Allergy Immunol* 2010; 21:586–94.
 - 15 Calvani M, Cardinale F, Martelli A *et al*. Risk factors for severe pediatric food anaphylaxis in Italy. *Pediatr Allergy Immunol* 2011; 22:813–9.
 - 16 Glaumann S, Nopp A, Johansson SG, Borres MP, Nilsson C. Oral peanut challenge identifies an allergy but the peanut allergen threshold sensitivity is not reproducible. *PLoS ONE* 2013; 8: e53465.
 - 17 Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 2001; 107:191–3.
 - 18 Bock SA, Munoz-Furlong A, Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001–2006. *J Allergy Clin Immunol* 2007; 119:1016–8.
 - 19 Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy* 2000; 30:1144–50.
 - 20 Pumphrey RS, Gowland MH. Further fatal allergic reactions to food in the United Kingdom, 1999–2006. *J Allergy Clin Immunol* 2007; 119:1018–9.
 - 21 Gallagher M, Worth A, Cunningham-Burley S, Sheikh A. Epinephrine auto-injector use in adolescents at risk of anaphylaxis: a qualitative study in Scotland, UK. *Clin Exp Allergy* 2011; 41:869–77.
 - 22 Uguz A, Lack G, Pumphrey R *et al*. Allergic reactions in the community: a questionnaire survey of members of the anaphylaxis campaign. *Clin Exp Allergy* 2005; 35:746–50.