

Prevalence of parentally perceived adverse reactions to food in young children

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A substantial number of parents perceive that their children have adverse reactions to food, but it is well documented that objective assessments agree with only one-quarter to one-half of parentally reported reactions. In order to prevent wrong diagnoses and curtail unnecessary or inadequate diets, primary health care providers need to deal with the parental perception of adverse reactions to food. A description of the prevalence and pattern of parentally perceived adverse reactions to food in children is needed to meet this challenge. The aim of the present study was to estimate the prevalence, incidence and cumulative incidences of parentally perceived adverse reactions to food in children younger than 2 years of age, and to study the duration of the reactions. A population-based cohort of 3623 children born in Norway was followed from birth until the age of two. At 6-month intervals, the parents completed questionnaires regarding the occurrence and type of any reaction to food. Information was available on the outcome measure at all age points for 77.4% of the families and these were used in the analyses; 3.8% of the cohort were entirely lost to follow-up. The cumulative incidence of adverse reactions to food was 35% by age two. Fruits, milk and vegetables accounted for nearly two-thirds of all reported reactions. Milk was the single food item most commonly incriminated, the cumulative incidence being 11.6%. The cumulative incidences of reported reactions to fruits and vegetables were 20.4% and 7.3%, respectively, with citrus fruits, strawberry and tomatoes as the most common food items in these groups. The cumulative incidences were less for food reactions associated with eggs (4.4%), fish (3%), nuts (2.1%) and cereals (1.4%). The duration of the reactions was short – approximately two-thirds of the reactions were not reported again 6 months later. However, the probability of remission depended on the food item concerned, the age at onset of reactions, and whether the reaction had been reported previously or not. Adverse reactions to food are reported by the parents of one-third of children in Norway before the age of two. The most striking feature of this study is the short duration of the food reactions, as approximately two-thirds of the reactions are not reported again 6 months later. Nevertheless, the high frequency of reactions attributable to milk is of concern. Milk is an important part of the Norwegian diet for children, and if removed from the diet its nutritional value is not easily replaced. Further studies are needed to assess the degree to which parents alter the diet of their children based upon perceived reactions to food.

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Adverse reactions to food arise from a variety of different mechanisms, either involving the immune system (allergies), physiological or enzymatic reactions (intolerances), or psychological mechanisms (1). In children, the onset of food allergy usually occurs before 2 years of age (2).

It is difficult to identify correctly an adverse reaction to food, primarily due to the diversity and subjectivity of symptoms and because the symptoms associated with food reactions are also characteristic of other childhood diseases. Further difficulties are due to a lack of under-

standing of the underlying pathogenesis of the disorder and the lack of simple objective means of assessment. The most reliable technique for confirming the diagnosis of an adverse reaction to food is the time-consuming and burdensome procedure of the double-blind placebo-controlled food challenge (DBPCFC). The difficulties the medical profession has with the concept and the diagnosis of adverse reactions to food means that parents venture into their own decision-making as to whether food causes symptoms in their children or not.

A substantial number of parents perceive that their children have adverse reactions to food. Estimates vary between 13 and 43% in pre-school children (3,4) and 4–13% in school children (3,5,6).

Use of the DBPCFC technique has revealed a discrepancy between parentally perceived reactions and objectively diagnosed reactions in their children as parents tend to over-estimate the role of food as the cause of symptoms in their children (4). This discrepancy is of concern for several reasons. Underlying illnesses may be missed due to a wrong focus on the origin of the disease. Further, children may be kept on unnecessary diets, which often are costly and may be disruptive in family meal planning and social life. Of even greater health concern is that elimination diets, whether appropriate or not, are potentially hazardous in terms of nutritional inadequacy (7,8). Although the specific causal factors are unknown, any of the factors outlined above may have contributed to the short height of school children with parentally reported food intolerances, reported in an English study (9).

Thus, primary healthcare providers need to handle parental perception of adverse reactions to food in order to prevent wrong diagnoses and curtail unnecessary or inadequate diets. A description of the prevalence and pattern of parentally perceived adverse reactions to food in children is needed to meet this challenge. The aim of the present study was to estimate the prevalence, incidence and cumulative incidences of parentally perceived adverse reactions to food, and further, to describe the natural history of the reported reactions, with special emphasis on the duration and the stability of reactions during the child's first two years of life.

Materials and methods

Study population

The study population included children born at the two main maternity clinics in Oslo, the capital city of Norway, during a 15-month period in

1992–1993. They were followed prospectively until the age of two, with the purpose of identifying risk factors for the development of allergic and obstructive diseases in childhood. The families had to meet the criteria shown in Fig. 1, to be included in the cohort. Exclusions were mainly due to language problems among immigrants, address outside Oslo and low birth weight. Of the 4973 families who met the criteria, 75% participated in the study. The study population is described in more detail elsewhere (10). Families from third-world countries were excluded from the present study (Fig. 1).

Responses to the questionnaires were obtained for 93%, 91% and 82% of the cohort at 12, 18 and 24 months, respectively. A total of 2803 families (77.4%) responded to all three questionnaires (Fig. 1). There was significant heterogeneity between the groups categorized by participation level, with respect to smoking during early pregnancy ($p < 0.001$), maternal age ($p < 0.001$), maternal education ($p < 0.001$), family income ($p < 0.001$) and birth weight of the children ($p = 0.001$) (Table 1). However, no differences were evident regarding maternal history of allergy ($p = 0.153$), percentage of first-born children ($p = 0.343$) or sex of the child ($p = 0.287$).

The Norwegian Data Inspectorate and the Regional Ethics Committee for Medical Research approved the study.

Data collection

The parents of the infants who were enrolled in the study were asked to complete a self-administered questionnaire on the maternity ward. Informed consent was obtained. Further information was collected by postal questionnaires addressed to the parents every 6 months until the child reached the age of two. The data collected when the children were 6 months did not include information on food reactions and are not used in the present analyses.

The operational definition of the outcome, parentally perceived reactions to food, was based on the following question addressed to the parents when the child was 12, 18 and 24 months of age: 'Does the child react to any food items? If yes, describe each reaction.' Possible symptoms were listed for the parents to mark off which symptoms the child had experienced. Furthermore, for each symptom, the parents were asked to indicate which food item they thought had caused the symptom (Appendix 1). The parents could add any symptoms not already mentioned. Food items were later classified into 10 groups: milk, egg, fish,

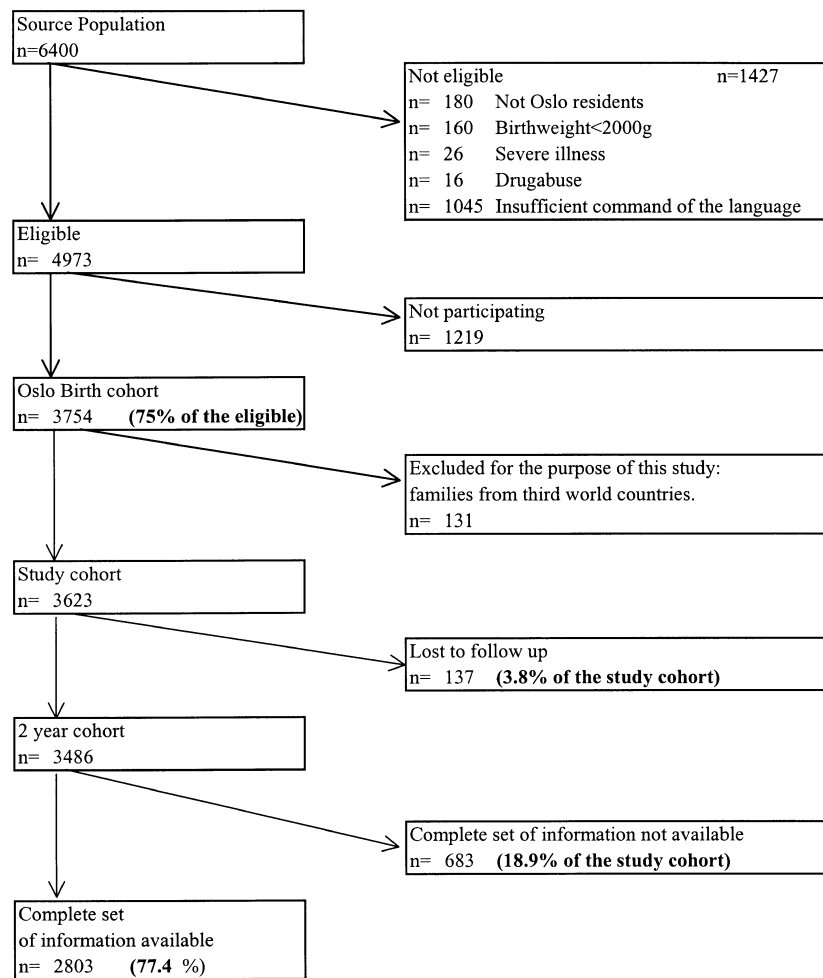


Fig. 1. Flow chart of the study population.

nuts, cereals, chocolate, fruits, vegetables, and others.

Information was collected on both non-participating as well as participating families by the midwives at the birth clinics regarding maternal smoking during pregnancy, maternal

allergy, maternal age, the sex of the child, whether the infant was the mother's first-born child, and birth weight of the child. Information on a wide number of background variables was obtained from the questionnaire completed by participating families at the maternity ward.

Table 1. Maternal smoking during pregnancy, maternal allergy, maternal age, maternal education in years, sex of the child, percentage of first-born children, birth-weight, and family income, according to number of completed questionnaires

	n	Mothers				Child					
		Smokers (%)	Allergy (%)	Age*	SD	Education*,†	SD	Gender (girl) (%)	No siblings (%)	Birth weight (g)*	Family income*,‡,§ (%)
Non-participants§	1044	42	19	29.1	5.0			46	53	3483	529
Participants: number of questionnaires answered											
None	137	44	13	28.7	5.3	12.8	2.9	47	46	3525	479
One	152	47	24	28.8	4.7	13.0	2.7	44	48	3575	527
Two	531	37	21	29.2	4.5	13.5	2.4	45	49	3565	514
All three	2803	32	20	30.2	4.5	13.9	2.4	49	52	3562	510

*p<0.001, other (non-significant) p values are given in the text.

†Information on maternal education and family income not obtained for non-participants.

‡Income <200 000 Norwegian kroner.

§Information available on 1050 out of 1219 non-participants, of whom third-world immigrants (n=6) were excluded.

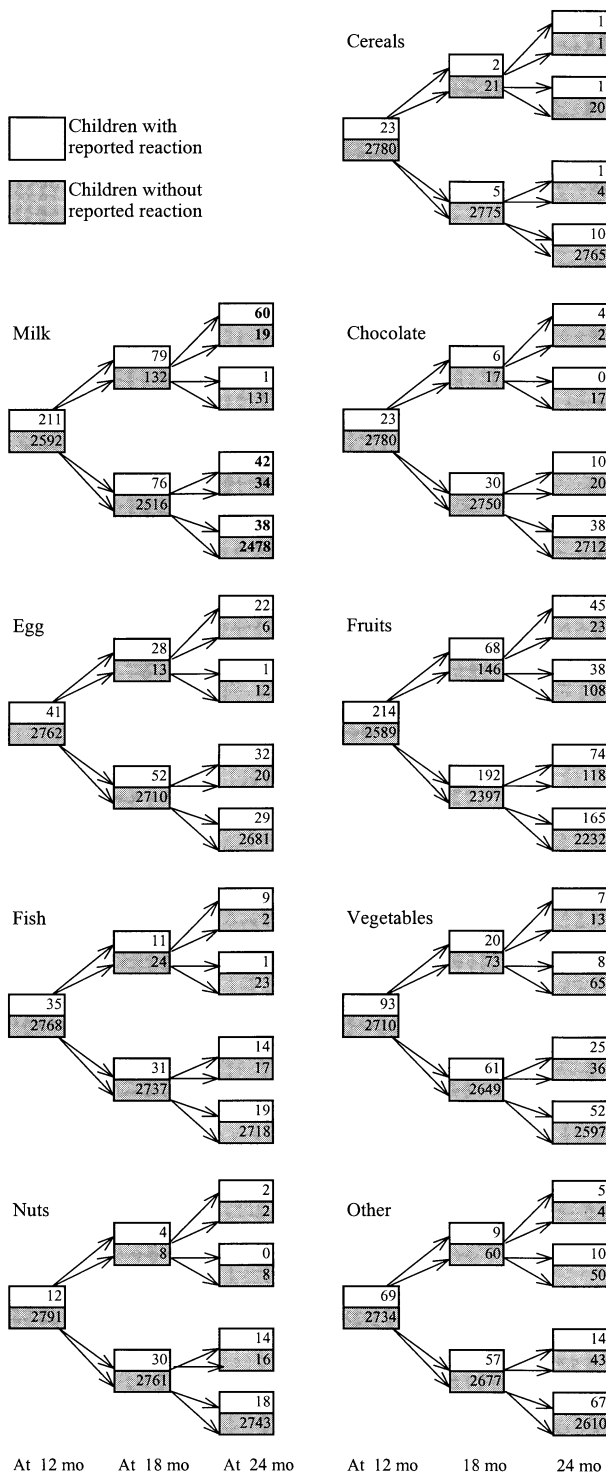


Fig. 2. Changes in reports of adverse reactions to different food items, in the course of time from 1 to 2 years of age.

Among these, socio-economic status was measured using mother's education in years and family income (greater or less than 200 000 Norwegian kroner).

Statistical analysis

All data were entered and partially analyzed by means of SPSS (Release 6.1). One-way analysis of variance (ANOVA) was used to test for mean differences in the continuously distributed data: birth weight of the children, maternal age and maternal education. Categorical data were presented in contingency tables and independence was tested by means of the Pearson χ^2 test. The prevalence of food reactions was calculated by dividing the number of positive reports to each food item by the number of completed questionnaires.

The confidence intervals were computed using the Wilson method (11):

$$\frac{(2np + z^2z \sqrt{z^2 + 4npq})}{2(n + z^2)},$$

where n denotes the sample size and p a single proportion, z denotes the standard normal deviate associated with a two-tailed probability and $q = 1 - p$.

This method is appropriate when the prevalence is low, or the study sample small (12). Incidence rates were estimated based on the number of children who had an onset of reaction every half year divided by the total number of children, and multiplied by two to obtain the incidence rate per year. The cumulative incidence was estimated as the number of reported reactions at either 12, 18 or 24 months divided by the total number of children.

Fig. 2 presents the data used for the analysis of probability of remission. The probability of remission was estimated for each food item. The percentage of children with a reported reaction (white boxes) at either 12 or 18 months and who later had no reaction (gray boxes) at 18 and 24 months, respectively, was calculated. Then percentages were calculated separately for children with different ages at onset. Finally the probability of remission was calculated depending upon how many times a reaction had been reported. Children with a reported reaction at 12 months and no reaction at 18 months, as well as children with a reported reaction at 18 months and no reaction at 24 months, were used to calculate a probability of remission for children for whom a reaction was reported only once. The numbers of children with a reported reaction at both 12 and 18 months were used to calculate a probability of remission for children for whom a reaction was reported twice (Table 4, column 5).

The stability of reactions to foods over time can also be appropriately assessed using estimated correlations between liability of reactions

Table 2. The prevalence of food reactions reported by those who completed all questionnaires compared with those who failed to complete one or two questionnaires

Number of questionnaires answered	Prevalence of reported food reactions					
	At 12 months*		At 18 months†		At 24 months‡	
	Responders	Food reaction (%)	Responders	Food reaction (%)	Responders	Food reaction (%)
All three	2803	533 (19.0)	2803	525 (18.7)	2803	585 (20.9)
Two	468	91 (19.4)	432	77 (17.8)	162	32 (19.8)
One	95	19 (20.0)	43	4 (9.3)	14	2 (14.3)
Total sample	3366	643 (19.1)	3278	606 (18.5)	2979	619 (20.9)

*p=0.952; †p=0.267; ‡p=0.788.

at different time points. An underlying continuous distribution is assumed for this liability, as measured by the dichotomous variable (either 'reaction' or 'no reaction') data. A reaction is assumed to be expressed whenever the individual liability reaches a certain threshold value. Tetrachoric correlations were calculated based on the two-way cross-tabulated tables of the food reactions at the different time points (13). The tetrachoric correlations were computed with the PRELIS computer program, which also estimates asymptotic standard errors of the correlations (14). The expectations for such correlations are identical with the expectations for Pearson correlations between the corresponding hypothetical underlying liabilities. The tetrachoric correlations do not depend on the threshold level for clinical reaction, nor on the prevalence of the reactions. Accordingly, estimates of the tetrachoric correlations between all time points are directly comparable even though the prevalence varies with age. The correlation pattern is informative in suggesting what type of mechanism causes the stability. The reactions may be primarily due to individual causal factors that are only acting during a limited period of the child's

life. Alternatively, they may be due to individual dispositions which affects a person's susceptibility throughout life, but which can usually only be observed as manifest problems during particular age periods in which children in general are relatively vulnerable. The first type of causality implies that relapse later in life is unlikely, whereas effects from more or less constant liability factors imply that a relapse is possible, especially if some of the factors associated with vulnerability during early childhood should recur. Correlations which decrease with time span, that is, higher values for t1–t2 and t2–t3 than for t1–t3, may suggest that the individual liability is highly age-dependent. Similar values for all points of time (t1–t2, t2–t3 and t1–t3) correspond with the notion of a relatively constant individual liability, which is augmented by some conditions (biological or environmental) shared by most children at a certain age period.

Results

The prevalence of adverse reactions to food as assessed by parental perception did not differ significantly between those who had answered

Table 3. Prevalence (%), incidence (rates per 100 person-years) and cumulative incidence (%) for parental reports of adverse reactions to food in 2803 children, with the 95% confidence intervals in parentheses

	Point prevalence			Incidence		Cumulative incidence At 24 months
	At 12 months	At 18 months	At 24 months	12–18 months	18–24 months	
Cow's milk	7.5 (6.6–8.6)	5.5 (4.7 to 6.4)	5 (4.3 to 5.9)	5.4 (4.6 to 6.3)	2.7 (2.2 to 3.4)	11.6 (10.5 to 12.8)
Hen egg	1.5 (1.1 to 2.0)	2.9 (2.3 to 3.5)	3 (2.4 to 3.7)	3.7 (3.1 to 4.5)	2.1 (1.6 to 2.7)	4.4 (3.7 to 5.2)
Fish	1.2 (0.9 to 1.7)	1.5 (1.1 to 2.0)	1.5 (1.1 to 2.1)	2.2 (1.7 to 2.8)	1.4 (1.0 to 1.9)	3 (2.5 to 3.7)
Nuts	0.4 (0.3 to 0.8)	1.2 (0.9 to 1.7)	1.2 (0.9 to 1.7)	2.1 (1.7 to 2.8)	1.3 (0.9 to 1.8)	2.1 (1.7 to 2.8)
Cereals	0.8 (0.6 to 1.2)	0.2 (0.1 to 0.5)	0.5 (0.3 to 0.8)	0.4 (0.2 to 0.7)	0.7 (0.5 to 1.1)	1.4 (1.0 to 1.9)
Chocolate	0.8 (0.6 to 1.2)	1.3 (0.9 to 1.8)	1.9 (1.4 to 2.4)	2.1 (1.7 to 2.8)	2.7 (2.2 to 3.4)	3.2 (2.7 to 4.0)
Fruits	7.6 (6.7 to 8.7)	9.3 (8.3 to 10.4)	11.5 (10.4 to 12.7)	13.7 (12.5 to 15.0)	11.8 (10.6 to 13.0)	20.4 (18.9 to 21.9)
Vegetables	3.3 (2.7 to 4.1)	2.9 (2.3 to 3.6)	3.3 (2.7 to 4.0)	4.4 (3.7 to 5.2)	3.7 (3.1 to 4.5)	7.3 (6.4 to 8.4)
Other	2.5 (2.0 to 3.1)	2.4 (1.9 to 3.0)	3.4 (2.8 to 4.2)	4.1 (3.4 to 4.9)	4.8 (4.1 to 5.6)	6.9 (6.0 to 7.9)
Any food item	19 (17.6 to 20.5)	18.7 (17.3 to 20.2)	21 (19.4 to 22.4)	19.3 (17.9 to 20.8)	13.5 (12.2 to 14.7)	35.4 (33.6 to 37.1)
One food	13.9 (12.7 to 15.2)	13.1 (11.9 to 14.4)	13.9 (12.7 to 15.2)	14.6 (13.3 to 15.9)	10.8 (9.7 to 12.0)	26.5 (24.9 to 28.2)
Two foods	3.9 (3.2 to 4.7)	3.7 (3.1 to 4.5)	4.6 (3.9 to 5.5)	3.5 (2.9 to 4.2)	2.1 (1.7 to 2.8)	6.7 (5.8 to 7.7)
More than two foods	1.2 (0.9 to 1.7)	1.9 (1.5 to 2.5)	2.3 (1.8 to 2.9)	1.2 (0.9 to 1.7)	0.6 (0.4 to 0.9)	2.1 (1.7 to 2.8)

only one, two or all three questionnaires (Table 2). The data used in all further analyses were confined to the 2803 families who responded to all three questionnaires (Fig. 1).

Milk

Milk was the food item most commonly incriminated. The prevalence of adverse reactions to milk, as assessed by parental perception, was 7.5% at 12 months of age. Subsequently the incidence rate as well as the prevalence decreased until 2 years of age (Table 3). This early peak in prevalence was typical for reactions to milk, otherwise found only in reactions to cereals. In Fig. 2, the consistency and the duration of the reported reactions to milk can be seen. The duration of reported reactions to milk was short and this is reflected by high probabilities of remission (Table 4). The probability of remission, however, depended on how long the reaction had lasted. If a reaction attributable to milk had been reported both at 12 and 18 months of age, the probability of remission (6 months later) was less than half that associated with a reaction that had been reported only once (Table 4). Additionally, the probability of remission depended on the age at onset. The probability of remission for a reaction to milk with onset at 18 months was significantly lower than for a reaction with an earlier onset. This effect, associated with age at onset, was most pronounced for milk, although the tendency was seen for other food items as well (Table 4). By the age of 24 months, as many as 11.6% of the parents had, at some point, attributed adverse reactions in their children to cow's milk.

Eggs

The prevalence of reactions to eggs at 1 year of age was 1.5%, but had doubled half a year later (Table 3). This rapid increase in prevalence was

also reflected by a high incidence rate between 12 and 24 months, whilst the probability of remission in the same period of time was low. The overall probability of remission was lower than for all other food items and particularly low when the reactions had been reported twice (Table 4). There was a non-significant trend towards lower probability of remission with an earlier onset of reaction. This was opposite to the trend found for reactions to other food items, where the probability of remission was usually higher for reactions with an early onset. The cumulative incidence of reactions to egg by 2 years of age was 4.4%.

Fish

Fish was reported as the offending food in 1.2% of all children at 1 year of age, increasing slightly over time. The reported reactions were of short duration, and only one-third of the reactions were reported more than once, although this depended on age at onset and number of times already reported (Table 4, Fig. 2). By the age of two, 3.0% of the children had had a reaction attributed to fish.

Nuts

Adverse reactions to nuts were uncommon before 1 year of age, but had increased threefold 6 months later (Table 3). The overall probability of remission for reported reactions to nuts was similar to that for milk (Table 4). The cumulative incidence of ever having had a reaction attributable to nuts before the age of 2 years was 2.1%.

Cereals

Six children (0.2%) were diagnosed with celiac disease before 2 years of age. They were not included here in the groups with reactions attributable to cereals or milk. Adverse reactions

Table 4. Remission of adverse reaction to food, during the next 6 months, as perceived by the parents

	Overall		Age of the child at time of onset				How many times the reaction had been reported			
			12 months		18 months		Once		Twice	
	%	CI	%	CI	%	CI	%	CI	%	CI
Milk	64	58–69	63	56–69	45	34–56	58	52–63	24	16–35
Egg	42	32–52	32	20–47	38	26–52	35	27–46	21	10–40
Fish	64	52–74	69	52–81	55	38–71	62	50–73	18	5–48
Nuts	62	47–75	67	39–86	53	36–70	57	42–71	50	15–85
Cereals	89	73–96	91	73–98	80	38–96	89	73–96	50	9–91
Chocolate	74	60–84	74	54–87	67	49–81	70	56–80	33	10–70
Fruit	61	57–66	68	62–74	61	54–68	65	60–70	34	24–46
Vegetables	74	67–80	78	69–86	59	46–70	71	63–77	65	43–82
Other	77	69–83	87	77–93	75	63–85	82	74–88	44	19–73

to cereals were uncommon. The highest prevalence, 0.8%, was found at 1 year of age (Table 3). Apart from milk, cereals were the only food for which the prevalence of adverse reactions was significantly less at 18 than at 12 months. The incidence rate between 1 and 2 years of age was low (Table 3). The probability of remission was higher for cereals than for any other food item (Table 4). The observed cumulative incidence of reactions to cereals by 2 years of age was 1.4%.

Chocolate

Adverse reaction to chocolate was reported in 0.8% of the children at 1 year of age, rising to 1.9% at 2 years of age (Table 3). The incidence rate of reactions attributable to chocolate increased with age and reached 2.7% between 18 and 24 months. The probability of remission was high, less than one-third of the reactions were reported again, and did not depend on the age at onset of the reaction (Table 4, Fig. 2). The cumulative incidence of reported reactions was 3.2% by the age of two.

Fruits

As a group, fruits were most commonly reported to cause adverse reactions. At 12 months of age, 7.6% of the children had had reactions attributed to a fruit and the prevalence increased with age and peaked at 11.5% at 2 years of age (Table 3). A wide variety of fruits were reported. Citrus fruits were mentioned particularly often, with a prevalence of 6.4% at 2 years of age. Other fruits commonly mentioned at 2 years of age were strawberries (2.6%), grapes (1.2%), apples (1.2%), kiwi fruit (0.7%), other fruits (1.2%) and other berries (0.9%) (data not tabulated). The incidence rate was highest between 12 and 18 months, a pattern seen for most other food items as well. There was no apparent difference in the prob-

ability of remission dependent on the time of onset of the reactions to fruit (Table 4). However, for a reaction reported twice previously, the probability of no reaction 6 months later was half that of a reaction reported only once previously (Table 4).

Vegetables

The prevalence of reactions attributed vegetables seemed stable. The vegetables most frequently reported were tomatoes (1.7%, data not tabulated). The overall probability of remission 6 months after the initial report was high if the reaction occurred before 1 year, and slightly lower when the initial onset was later (Table 4). In contrast to other reactions to food, the probability of remission did not seem to be influenced by how many times the reaction had been reported previously (Table 4). The cumulative incidence of reactions to vegetables by 2 years of age was 7.3% (Table 3).

Other foods

This group consists of reactions attributable to one of the following food items: additives, sugar, caviar, meat, shrimps, or soy. Soy is included in 'other', because it is very rarely mentioned. Only four parents attributed reactions in their children to soy (0.1%). The prevalence of reactions to any one of these foods was 2.5% at 12 months of age, and increased with age. Within this group, additives were most common, mentioned in half the cases, with a point prevalence of 1.8% at 2 years (data not tabulated). Reactions to different sorts of meat and shrimps were mentioned equally often, with 0.5% prevalence at 2 years of age. The prevalence of reactions to caviar and sugar reached 0.3%. The incidence rate of reported reactions to this group of food items peaked late, between 18 and 24 months, a pattern similar to reactions to chocolate (Table 3). This was in contrast to reactions to most food items, where incidence rates declined after 18 months.

Any foods

The prevalence of reactions to any type of foods or liquid was 19% (533 children) at the age of 12 months and remained stable during the next year. Among those who reacted adversely to food, most were believed to react to only one item, whereas 3.9% of the children were reported to react to more than one food item at 12 months, and the percentage increased slightly with age as shown in Table 3.

Table 5. Tetrachoric correlations between the prevalence of reported reaction to a food at different age points with asymptotic standard errors of the correlations in parentheses. t1 represents 12 months, t2 18 months and t3 24 months

	t1-t2 (SE)	t2-t3 (SE)	t1-t3 (SE)
Milk	0.73 (0.03)	0.93 (0.02)	0.63 (0.04)
Egg	0.86 (0.03)	0.93 (0.02)	0.77 (0.05)
Fish	0.70 (0.07)	0.89 (0.03)	0.67 (0.08)
Nuts	0.65 (0.11)	0.86 (0.04)	0.47 (0.15)
Cereals	0.63 (0.15)	0.71 (0.14)	0.52 (0.15)
Chocolate	0.63 (0.10)	0.73 (0.06)	0.45 (0.12)
Fruits	0.48 (0.04)	0.63 (0.03)	0.51 (0.04)
Vegetables	0.55 (0.06)	0.72 (0.05)	0.42 (0.07)
Other	0.40 (0.09)	0.57 (0.06)	0.48 (0.07)
All reactions	0.59 (0.03)	0.75 (0.02)	0.53 (0.03)

Tetrachoric correlations

High correlations were found for most food items between all measured time points, with especially high correlations found for the food items milk, egg, and fish (Table 5). The tetrachoric correlations decreased with time for all reported food reactions considered, with the exception of the group 'other', where a constant correlation was seen. The decrease in the correlations over time (lower values for t1–t3 than for t1–t2 and t2–t3) was most marked for milk and least for fruits.

Discussion

The main finding in our study is that one in every third child is reported to have had adverse reactions to food before 2 years of age. The most striking feature is the short duration of the reactions, as approximately two-thirds of the reactions are not reported again 6 months later. However, the probability of remission depends on the food item concerned, the age at onset of reactions, and whether the reaction has been reported previously or not. Fruits, milk and vegetables account for nearly two-thirds of all reactions.

Validity of results

The estimates are based entirely on the perceptions of the parents. No attempt has been made here to classify the reactions into probable or uncertain reactions as has been done in some studies (5,6). It is well documented that objective assessments agree with only one-quarter to one-half of parentally reported reactions (4,15).

The outcome measure is subject to random error associated with the degree of certainty upon which the parents base their perception, as well as the severity of the reaction and the length of time since the last observation.

This study has a longitudinal design, collecting information retrospectively from the last 6-month period every 6 months, which gives the period prevalence, even though the question itself asks for the point prevalence at each age. We have assumed that the point prevalence at each age point approximates the period prevalence for the past 6 months.

A food reaction characterized by an early onset and quick development of tolerance may be missed, as there is no information on the outcome measure during the first 6 months. Although reactions may occur in the exclusively breast-fed, especially to cow's milk and egg proteins transferred through the breast, the onset of adverse reactions to food largely depends on

the age at which solid foods are introduced. As the majority of mothers in Norway breast-feed for at least 6 months (16), the expected onset of the reactions is after 6 months. Furthermore, although unconfirmed reactions have been found to have a duration as short as 2 months, the median duration of confirmed reactions is seldom found to be less than 9 months (4,17). The lack of information during the first 6 months is thus unlikely to influence our estimates substantially.

The results are based on an urban Norwegian population. There may be prevalence differences in food allergy between rural and urban areas, however there is no knowledge about this.

Selection bias may arise due to differences between the source and the study population. There may be differential exclusion of families due to (1) the inclusion criteria set by us (2), differences between the eligible but non-participating families and the participating families, and (3) the fact that the families lost to follow-up may differ from the families who continue to participate.

Residents with plans to move out of the city were excluded. It may be assumed that families with plans to move may want to do so because of a known susceptibility to atopic disorders. Children with birth weight less than 2500 g were excluded. Prematurity is believed to increase the risk for food allergy, due to immaturity of the bowel mucosa as well as the immunological defense system. Thus, the exclusion of families due to plans for moving or low birth weight could result in a slight bias whereby the prevalence is under-estimated. The numbers of families excluded due to drug abuse ($n = 16$) or severe illness ($n = 26$) are too small to have any impact.

To assess possible bias associated with non-participants ($n = 1219$), information was collected by the midwives for all the families at the birth clinics. The proportion of smokers was higher among non-participants (Table 1), but the impact of this is unknown. Non-participating families reported slightly less maternal allergy than the participating families, but this difference was not significant.

There may be selection bias associated with loss to follow-up. There was a higher proportion of smokers and families from a lower social class, as reflected in a shorter maternal education in years and a lower family income, among those lost to follow-up. It is uncertain how this affects the validity. A previous study reported greater prevalence of reported adverse reactions to food among children whose parents were well-educated (5). On the other hand, a study based on an adult population revealed no association between

confirmed reactions to food and occupational category (18).

Parents with susceptible children may feel a stronger obligation to participate. However, atopic disease may be a burden on the family leading to a higher likelihood of dropping out of the study. Judging by the proportions of families with reported maternal allergy, there is no significant difference in atopic risk between participants and those lost to follow-up in this study.

Analyses based on families responding to all questionnaires, compared to those based on families who responded to only one or two questionnaires, show no significant differences in the prevalence of reported food reactions (Table 2). This suggests minimal effects of selection bias associated with loss to follow-up in this study.

Synthesis with previous knowledge

Previous studies of parentally perceived adverse reactions to food in young children report estimates of a similar magnitude as those in this study. In a prospective population-based study in the USA, 28% of 480 children were suspected by the parents or physicians to have had adverse reactions to food during their first 3 years of life (4). These estimates are comparable to the cumulative incidence at 2 years of age of 35.4% found here. Our prevalence estimates are very similar to a Finnish cross-sectional study. They reported the prevalence of parentally perceived adverse reactions to food in 866 children, randomly selected at the well-baby centers. The point prevalence was 19% at 1 year and 22% at 2 years of age (3), which is very similar to our prevalence estimates. Lower prevalence estimates have been reported for children aged 5–6 (3.8–8%) (3,6) and 5–11 (4%) (5). This follows the expected pattern for prevalence of adverse reactions to food, which declines with age.

There is a remarkable similarity across studies in the pattern of food items reported by the parents to cause complaints. In all studies, the proportion of children with complaints about milk, fruits and vegetables is high (3,4). Within the group of fruits and vegetables, the same foods, citrus and tomatoes, are most commonly reported and responsible for 50% of all reactions within the group.

However, our results differ in some aspects. Milk is by far the most common single food item incriminated by the parents of Norwegian children. Adverse reactions to milk have an early onset and the reported prevalence at

1 year of age is as high as 7.5%. This is in contrast to the study from Finland, where only 2% reported reactions to milk at 1 year of age. However, at 2 years of age, the prevalence was similar (5.5% in Norway, 5% in Finland). The reason for the apparent late age at onset of reactions to milk in Finland is uncertain. As it is the age at which the parents recognize the causal role of food which is reported, low public awareness of adverse reactions to food could result in a lag in reported age at onset. Clinical experience supports an early onset of reactions attributable to milk as found in our study. Several studies of adverse reactions to cow milk report that the prevalence of confirmed reactions is between 2 and 3% among 1-year-old children (17,19,20). As these are objectively confirmed reactions, estimates based on parental perception would presumably be much higher, supporting our results.

There is a differential pattern among the food items thought to cause a reaction in Europe compared to North America. Reported reactions to fish are almost as common as for eggs in Norway. This phenomenon was also found in Finland where the prevalence of reactions to fish was even higher (3) and in Spain (21). In contrast, adverse reactions to fish are rare in North American countries (4,22). However, reactions to soy and nuts are rarely reported in Norwegian and Finnish children (3), while they are among the four food items most commonly reported in North America, surpassed only by milk and eggs (4). A higher frequency of soy intolerance is reported in studies where soy-based formulas have been used as dietary supplements for children who have adverse reactions to cow's milk (19,22) than in studies where cow milk-based hydrolysates have been used as dietary supplements (23). These results suggest that differences in dietary habits may explain part of the variation between countries in terms of which food items elicit adverse reactions.

With a few exceptions, the incidence rates for most food items tended to decline after 18 months. This finding is in agreement with population-based studies (4), as well as clinical studies on serum immunoglobulin E responses to common food proteins in childhood (24).

Some previous studies have reported a peak incidence before 1 year of age, and few onsets of reactions to food after 1 year of age (4). This is in contrast to our results where many reactions occur after the age of one, and is probably explained by the late weaning practice in Norway (16). Likewise, differences in custom of when different food items are usually given for the first

time probably explain the early peak incidence of reactions to milk and cereals and the later incidence peak of reactions to chocolate.

The short duration of the reactions found in this study is in agreement with a previous study estimating the duration of both confirmed and unconfirmed reactions, in which the median duration for reactions classified as confirmed was 9 months and 2 months for the unconfirmed reactions (4).

We expect that the lower probability of remission if a reaction was reported twice is due mainly to a higher degree of reactions being correctly associated with food in the group with repeated reports. Some (19,22), but not all (23), previous studies on the probability of remission of confirmed reactions to milk support the finding of a higher probability of remission during the first year than the following years.

As we have data from only three time points, all the children with repeatedly reported reactions (Table 4, column 5) have the same age at onset (12 months). A longer observation period would be needed to fully disentangle the effect of the duration of the reaction from the effect of the age at onset on the probability of remission.

The decrease in the tetrachoric correlations with time for all reported food reactions considered suggests that the liability of a food reaction is to some extent influenced by specific individual age-related factors, and gives a further indication of a high probability of remission with time. However, the tetrachoric correlations give some further information. Among the food groups with a very high probability of remission, not all have a marked decrease in the tetrachoric correlations with time. For instance, fruits have a better short-term probability of remission than milk, reflected both in the higher percentage of probability of remission in Table 4 and a lower tetrachoric correlation in Table 5. However, the decrease in the correlations over time is not so pronounced as for instance in milk. This indicates that the individual disposition to react to fruits is more stable and constant, and that even though the short-term probability of remission is very high, in the long run the tendency to react to fruit may be more persistent. The cross-time correlations were constant only for the food group labeled 'other', and as this group consists of unrelated food items, the correlations should not be interpreted.

The very high probability of remission reported for nuts and fish, food allergens usually associated with a lower probability of remission than for egg and milk, is puzzling. Our finding could be due to imprecision in the measured outcome. Fish

and especially nuts are well-recognized food allergens and may be blamed unjustly when the offending agent is unknown or the symptom is not related to food at all. As unjustly blamed food reactions, associated with random influences, are unlikely to recur, the probability of remission will be high. Apart from this, the other results for the probability of remission were in good agreement with those from clinical studies, with the lowest remission rate being for egg.

Conclusion

This study estimates prevalence, remissions and cumulative incidences of adverse reactions to foods in children, as reported by the parents, at regular intervals. Compared to previous studies, random error attributable to sampling variation is reduced in this study, due to the large sample size. Furthermore, due to the relative small loss to follow-up, potential selection bias is also reduced here when compared to studies with similar designs and study populations.

The perception of whether symptoms the child may have are due to food or not is often highly subjective, and affected by a variety of factors, such as the media profile on the topic and the prevalence in the community of chronic diseases such as atopic eczema. In this context, it is remarkable that the estimates based on parental perception show such a consistent pattern across different studies.

The most striking feature of this study is that most of the food reactions have a very short duration, lasting less than 6 months. To our knowledge this is the first study to assess the duration of parentally perceived reactions.

This study focuses on the prevalence of parentally reported adverse reactions to food among children. Two broad issues deserve to be further explored. First, while it has not been addressed here, studies assessing the validity of parental reports are needed to estimate the prevalence of objectively proven adverse reactions to food. Second, regardless of the validity of the parental perception, it is of concern that food is commonly perceived as being the cause of symptoms in children because their diets may then be altered. Some food items, such as milk, are an important part of the Norwegian diet, and if removed from the diet the child's nutritional needs may not be met. Further studies are needed to assess the degree to which parents alter the diet of their children based upon perceived reactions to food.

Our results reveal that parental perception of adverse reactions to food is substantial and may

therefore have important consequences for children's health.

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Appendix 1.

Does the child react to any food items

- ☐ Yes, if yes describe the reaction by marking off for each symptom
- ☐ No

Type of reaction	Caused by
☐ Breathing problems	☐
☐ Vomit	☐
☐ Diarrhea	☐
☐ Stomach pain	☐
☐ Rashes	☐
☐ Irritability	☐
☐ Other reactions, what:	☐