FOOD CONSUMPTION DURING INFANCY AND EARLY CHILDHOOD AND ATOPIC SENSITIZATION AT THE AGE OF 5 YEARS

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M.Sc. thesis
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May 2014

UNIVERSITY OF EASTERN FINLAND, Faculty of Health Sciences, Clinical nutrition
HÄMÄLÄINEN, NIINA J.: Food consumption during infancy and early childhood and atopic sensitization at the age of 5 years.
Master's thesis, 59 p.
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May 2014

Keywords: allergy, atopy, child, diet, food, immunoglobulin E, infant

FOOD CONSUMPTION DURING INFANCY AND EARLY CHILDHOOD AND ATOPIC SENSITIZATION AT THE AGE OF 5 YEARS

Background: Allergic diseases have become a major health concern over the last decades particularly among children. One of the main hypothesis is, that dietary changes might have led to the increase in the prevalence. Several studies have examined the intake of specific nutrients in the early childhood in relation to the development of allergic diseases, but studies on food consumption are rare. Moreover, studies with longitudinal follow-up and the association between food consumption and allergies have not been conducted widely.

Aim of the study: The aim of this thesis was to study whether food consumption during infancy and early childhood affects the risk of atopic sensitization at the age of 5 years.

Subject and methods: This study is based on data from the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study, a population based birth cohort study of type 1 diabetes genetically-susceptible children. The current study population comprised of 1928 5-year old children from Tampere region. Data on food consumption was collected by means of dietary records at 3 and 6 months and 1, 2 and 3 years of age. Specific immunoglobulin E (IgE) antibodies to four food (egg, cow's milk, fish, wheat) allergens and four inhalant (house dust mite, cat, timothy grass, and birch) allergens were measured at 5 years of age. In the present study the endpoints were atopic sensitization to any allergen, any food allergen and any inhalant allergen. Logistic regression was used to analyze the association between food consumption and the endpoints at each time point (3 and 6 months, 1, 2 and 3 years), adjusting for potentially confounding factors and total energy intake.

Results: Overall 36.9 % of the study population were sensitized to any allergen, 23 % to any food allergen and 26 % to any inhalant allergen. In this study, the consumption of oat/barley (6 months, 1 and 2 years), rye (6 months, 1 and 3 years), wheat (6 months, 1, 2 and 3 years), potatoes/roots (6 months and 1 year), egg (1, 2 and 3 years), fish (1 and 2 years) and cow's milk (3 years) were associated with decreasing risk of atopic sensitization. Consumption of other cereals (rice, buckwheat, corn flour and millet) at the ages of 6 months and 1, 2 and 3 years were associated with increased risk of atopic sensitization.

Conclusion: Overall, a novel finding of this study is the reduced risk of atopic sensitization with the consumption of oat, barley, rye and wheat, which are common cereals used in Finland. The reduced risk of atopic sensitization with cow's milk and fish consumption is consistent with previous findings. These results support increasing suggestions that diet may play a role in the primary prevention of allergic diseases. However, more studies with longitudinal follow-up are needed on this topic to make further conclusions and possible recommendations.

ITÄ-SUOMEN YLIOPISTO, Terveystieteiden tiedekunta, Kliininen ravitsemustiede

HÄMÄLÄINEN, NIINA J.: Varhaislapsuuden ruuankäytön yhteys atooppiseen herkistymiseen 5-vuotiaana.

Pro gradu –tutkielma, 59 s.

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Toukokuu 2014

Avainsanat: allergia, atopia, immunoglobuliini E, lapsuus, ruokavalio, ruuankäyttö, varhaislapsuus

VARHAISLAPSUUDEN RUUANKÄYTÖN YHTEYS ALLERGISEEN HERKISTYMISEEN 5-VUOTIAANA

Tausta: Allergisista sairauksista on viime vuosikymmenten aikana tullut merkittävä kansanterveydellinen ongelma. Vallitseva hypoteesi on, että muuttunut ruokavalio on syynä allergisten sairauksien lisääntyneeseen esiintyvyyteen. Useat tutkimukset ovat tarkastelleet ravintoaineiden yhteyttä allergisten sairauksien kehittymiseen, mutta tutkimukset ruoka-aineilla ovat harvinaisempia. Pitkittäisiä seurantatutkimuksia ruuankäytön ja allergisten sairauksien yhteydestä ei ole laajalti tehty.

Tavoitteet: Tämän tutkimuksen tavoitteena oli tutkia varhaislapsuuden ruuankäytön yhteyttä atooppiseen sensitiivisyyteen 5-vuotiaana.

Aineisto ja menetelmät: Tutkimuksen aineistona käytettiin suomalaisen Tyypin 1 diabeteksen ennustaminen ja ehkäisy tutkimuksen (DIPP) ravintotutkimuksen aineistoa. DIPP on syntymäkohorttitutkimus, johon osallistui lapsia, joilla on geneettinen alttius tyypin 1 diabeteksen kehittymiselle. Tutkimuksen lopullinen aineisto koostui 1928 Tampereen alueella asuvasta 5-vuotiaasta lapsesta. Tiedot ruuankäytöstä on kerätty aiemmin ruokapäiväkirjojen avulla 3 ja 6 kuukauden iässä, sekä 1, 2 ja 3-vuotiaana. Yksityiskohtaiset immunoglobuliini E (IgE) vasta-ainemääritykset neljälle ruoka-allergeenille (kananmuna, lehmänmaito, kala, vehnä) sekä neljälle inhalaattiallergeenille (pölypunkki, kissa, timotei, koivu) on mitattu 5-vuotiaana. Tässä tutkimuksessa vastemuuttujina olivat: atooppinen sensitiivisyys mille tahansa allergeenille, mille tahansa ruoka-allergeenille ja mille tahansa inhalaattiallergeenille. Ruuankäytön ja atooppisen sensitiivisyyden yhteys analysoitiin jokaisessa ikävaiheessa (3 ja 6 kuukautta ja 1, 2 ja 3 vuotta) erikseen. Tulosten analysointiin käytettiin logistista regressioanalyysiä. Tulokset vakioitiin mahdollisten sekoittavien taustatekijöiden sekä kokonaisenergiansaannin suhteen.

Tulokset: Kaikkiaan 36,9 % tutkimukseen osallistuneista lapsista oli herkistynyt vähintään yhdelle allergeenille, 23 % vähintään yhdelle ruoka-allergeenille ja 26 % vähintään yhdelle inhaalaattiallergeenille. Yhteys atooppisen herkistymisen pienentyneeseen riskiin löytyi seuraavista ruoka-aineryhmistä: kaura/ohra (6 kk, 1 ja 2 v), ruis (6 kk, 1 ja 3 v), vehnä (6 kk, 1, 2 ja 3 v), peruna/juurekset (6 kk ja 1 v), kananmuna (1, 2 ja 3 v), kala (1 ja 2 v) ja lehmänmaito (3 v). Muiden viljojen (riisi, tattari, maissijauho ja hirssi) käyttö 6 kuukauden sekä 1, 2 ja 3 vuoden iässä oli yhteydessä lisääntyneeseen atooppisen herkistymiseen.

Johtopäätökset: Tässä tutkimuksessa havaittua käänteistä yhteyttä yleisesti Suomessa käytössä olevien viljojen; kauran, ohran, rukiin ja vehnän käytöstä atooppiseen herkistymiseen ei ole aiemmin raportoitu. Havaittu lehmänmaidon ja kalan käytön yhteys pienentyneeseen herkistymisriskiin on linjassa aiemman tutkimusnäytön kanssa. Tulokset vahvistavat kasvavaa käsitystä ruokavalion merkityksestä allergisten sairauksien primaari preventiossa. Kuitenkin lisää pitkittäisiä seurantatutkimuksia ruokavalion ja allergioiden yhteydestä tarvitaan, jotta voidaan tehdä laajempia johtopäätöksiä sekä mahdollisia suosituksia.

"Success is the ability to go from one failure to another with no loss of enthusiasm."

Winston Churchill

CONTENTS

1 INTRODUCTION

The prevalence of allergy and allergy-related diseases, such as atopic eczema, allergic rhinitis and asthma, has increased in the recent decades, especially in industrialized countries (Devereux 2006). The number of people suffering from these conditions worldwide is huge, and the raising concern over the past decades has been the possible effect the lifestyle factors might have on the development of allergic diseases. It has been hypothesized, that changes in our diet might be one of the main reasons for the increase in the prevalence (Seaton et al. 1994, Black and Sharpe 1997, Fogarty and Britton 2000). Suggestions have been made that the decreased intake of antioxidants and n-3 polyunsaturated fatty acids (n-3 PUFA) and increased intake of n-6 polyunsaturated fatty acids (n-6 PUFA) might have an important role in the allergy development (Seaton et al. 1994, Black and Sharpe 1997, Fogarty and Britton 2000). This leads to the assumption that fruit, vegetables and fish particularly might be the key factors in our diet. Overall, different dietary factors have been suggested to play different roles in the development of allergic diseases.

Most food allergies develop during the first year of life (Hong and Wang 2012), emphasizing the importance of early life dietary exposures, as a critical time period in the early life for the development of food allergies truly exists. Since diet is a modifiable exposure, if its role in the development of allergies is confirmed, it provides an opportunity to develop key strategies for the early life primary prevention of allergy in children.

Although studies of food consumption in early childhood and allergies are rare, few studies have found that fish consumption in early childhood is associated with a decreased risk of developing allergies or asthma later in child’s life (Dotterud et al. 2013, Kull et al. 2006, Nafstad et al. 2003, Oien et al. 2010). Cow’s milk, unprocessed cow’s milk especially, has been associated with reduced risk of asthma, allergic rhinitis, and sensitization to pollen and some food allergens. Some inverse associations between egg consumption and allergic rhinitis and fruit and vegetable consumption and asthma and allergic rhinitis have also been reported (Waser et al. 2007, Rosenlund et al. 2011, Lepski and Brockmeyer 2013).

Most studies investigating the association between diet and the development of allergy in childhood have studied the intake of specific nutrients. Apart from few studies highlighted above on fish and cow’s milk consumption and some studies looking at the impact of timing of infant feeding, studies investigating the actual food consumption during infancy and early childhood in the development of allergy later in the child’s life are rare. In addition, the evidence at the moment is lacking on the role of longitudinal dietary exposure during infancy and early childhood in allergy development in childhood.

The main aim of this study was to investigate the association between food consumption during the first 3 years of life and the development of IgE-sensitization at 5 years of age. In this study, the intention was to investigate large food groups to get an extensive look at whether diet is associated with the development of IgE-sensitization.

2 REVIEW OF THE LITERATURE

2.1 The prevalence and burden of asthma and allergy in childhood

Allergy and allergy related diseases such as atopic eczema, allergic rhinitis and asthma, have become a major public health concern worldwide (Devereux 2006, Pawankar et al. 2011). The high prevalence of allergic diseases has generally been a problem in developed countries, yet these conditions have become so dramatically common that they now form a large problem in developing countries as well (Pawankar et al. 2011). Increase in the prevalence mostly appears with children and the young, and therefore sets a considerable challenge for the future (Pawankar et al. 2011).

According to World Health Organization (WHO) (Pawankar et al. 2011) 30-40 % of the world population suffer from allergic diseases and 40 % have atopic sensitization. Food allergy and asthma figures are huge, 220-250 million and 300 million, respectively. These numbers are estimates, but give some idea of the magnitude of the prevalence of these conditions. Among children and adolescents, allergic diseases are the most common occurring chronic disorders. Majority of food allergies present in the early childhood are outgrown, but this does not seem to be the case with other allergic conditions (Haahtela et al. 2008). Allergic symptoms differ greatly between individuals and there is no straightforward tendency of how the symptoms might develop, since they might spontaneously resolve permanently or worsen again after being mild or non-existent for some time. Although most allergic symptoms are mild and not life-threatening, the burden for patients and overall annual costs for the health care systems are significant (Haahtela et al. 2008).

In Finland, especially allergic diseases and symptoms involving the respiratory system are fairly common (Table 1). In a Finnish study (Nwaru 2012) 30% of the study population were sensitized to some allergen (n = 1018). Of those, 23% sensitized to inhalant allergens and 17% to food allergens. In 2005, the annual costs of asthma in Finland were €230 million and direct costs of allergies and asthma combined were €348 million (Haahtela et al. 2008). The costs have since been reduced, but are still 3% of overall health care costs in Finland. One of the main goals of the Finnish Allergy Programme, launched in 2008, is to reduce the costs by 20% by the year 2018 (Haahtela et al. 2008) (Table 2). For this reduce to be possible, changes in treatment and prevention of allergic conditions are inevitable. The researchers at the program conclude, that tolerance to allergens can be strengthened and possibly restored by exposing allergic individuals to the symptom causing allergens. Increasing immunological tolerance is the main aim of the program and sets a promising starting point, not only in prevention but also in reducing the symptoms and successfully preforming desensitization when conceivable. The main goals of the program are listed in table 2.

Table 1. The estimated prevalence of allergic conditions in Finland in the 2000s (Haahtela et al. 2008).

ALLERGIC CONDITION	**%**
Adult asthma	8-10
Childhood asthma	5
Asthma-like symptoms	5-10
Allergic rhinitis (seasonal and perennial)	30
Hay fever (pollen allergy)	20
Allergic conjunctivitis	15
Atopic eczema	10-20
Urticaria	7
Contact dermatitis	8-10
Food allergy (adults)	2-5
Food allergy (children)	5-10
Drug hypersensitivity	2
Insect hypersensitivity	2
Light hypersensitivity	15-20
Allergy to animals	15
At least one positive SPT[1] result (adults)	47
Allergy in family	30
Use of asthma or allergy medication (past 12 months)	35

1 SPT = skin prick testing

Table 2. The main goals of the Finnish allergy programme 2008-2018 (Haahtela et al. 2008).

- To prevent the development of allergy symptoms: prevalence of asthma, allergic rhinitis and atopic eczema is decreased by 20%.
- To increase tolerance against allergens: number of subjects on elimination diets caused by food allergy are decreased by 50%.
- To improve allergy diagnostics: all patients are tested in quality certified allergy testing centers.
- To reduce work-related allergies: allergic diseases defined as occupational are decreased by 50%.
- To allocate resources to manage and prevent exacerbations of severe allergies: "allergy control cards" are in use in the whole country and emergency visits caused by asthma are decreased by 40%.
- To decrease costs due to allergic diseases: predefined costs are reduced by 20%.

The treatment and medication for allergic conditions is not ideal in most countries and only a few countries have extensive medical services to comprehensively treat allergic diseases. Allergic symptoms and conditions are not generally well understood and in the lack of proper clinical services, patients seek alternative non-scientific remedies. This might not only be useless waste of time and money, but potentially harmful for the patient. In light of this, World allergy organization (WAO) has set to promote the clinical care education and research for the better treatment and diagnosis for allergic diseases. WAO emphasizes the importance of researching the causes and management in the field of allergy in order to provide effective prevention strategies and more targeted treatments. In the Finnish Allergy Programme it is also mentioned that promoting the development of overall better and more effective treating practices, for example by supporting health instead of medicating, is important (Haahtela et al. 2008).

2.2 Possible risk factors for allergy in children

The environment where people live has dramatically changed over the last decades. Early life exposures to different antigens have become rare when people have moved from countryside to urban habitats. In addition, the modern diet has become more unbalanced and one sided, which has limited the antigen exposure even further. Unbalanced and one sided diet also promotes the development of low grade inflammation which has been associated with allergy development among other chronic noncommunicable diseases (Haahtela et al. 2008, Prescott 2013). Understanding of these factors has led to several hypotheses of the possible effect environmental factors (e.g. diet, pollution and hygiene) might have in the increase of the prevalence of a several noncommunicable diseases including allergic conditions (Devereux 2006).

In the review of IgE-mediated food allergy in children, Longo et al. (2013) mention the implications of substantial long-term disease burden for children with persistent allergies and those with high concentrations of cow's milk, egg and wheat IgE measured from blood samples. The researchers point out that previous guidelines for the treatment and prevention of allergies with high risk infants (infant with at least one parent with allergic condition) recommended delayed introduction of high allergenic foods (e.g. egg, cow's milk and wheat) and other antigen avoidance. Recommendations were based on the concerns that young infants may have increased risk of developing allergic reactions because of the immature mucosal immunity and increased gut permeability (Palmer and Prescott 2012).

As it is now well known, late introduction of solid foods was found ineffective and even potentially harmful by increasing the risk of allergy development (Heine and Tang 2008, Hong and Wang 2012, Longo et al. 2013). Studies conducted in the past 5 years support these conclusions as they have shown that early contact with food can induce tolerance and prevent sensitization to foods (Longo et al. 2013). However, preliminary results of ongoing randomized controlled trials suggest that considerable proportion of infants have established sensitization and clinical reactivity prior to the introduction of solid foods (Palmer and Prescott 2012, Palmer et al. 2013). This indicates that maternal diet during pregnancy and lactation might have a substantial role in atopic sensitization for at least with some infants.

Overall, the mechanisms in which diet might affect the risk of allergy are still partly unclear. It seems however, that diet influences the immunological development trough intestine (Molloy et al. 2013). The intestine's mucosal flora develops when different food antigens are introduced to it and there are indications that a critical time period for this allergen exposure exists. It has been suggested, that due to the mucosal flora developing in certain way, it does not recognize certain antigens in foods as "friendly" if the critical time period is passed, and therefore the risk for the development of allergic diseases increases highly (Hong and Wang 2012, Longo et al. 2013).

2.3 The mechanisms of IgE mediated allergic reaction

In a majority of cases allergic sensitization is the result of immunoglobulin E (IgE) mediated immune responses to allergen exposure (Burks et al. 2012). Allergic reaction develops when the body is exposed to harmless environmental antigens. Normally, the immune system differentiates the body's own cells from foreign ones and harmless from harmful. In an allergic reaction, the immune system is for unknown reason "misreading" the situation and identifies harmless antigens as harmful. This leads the body to start to produce IgE, as to fight the invading substances (Lepski and Brockmeyer 2013).

IgE mediated allergic reaction is induced by cytokines (e.g. IL-4, IL-5 and IL-13) released by T-helper 2 (Th2) cells that lead B lymphocytes to differentiate to plasma cells that produce IgE (Burks et al. 2012). The production of IgE triggers the release of histamines, leukotrienes and other transmitters that cause allergic symptoms, such as swelling and itching (Lepski and Brockmeyer 2013). The pathway of IgE mediated allergic reactions is presented in figure 1.

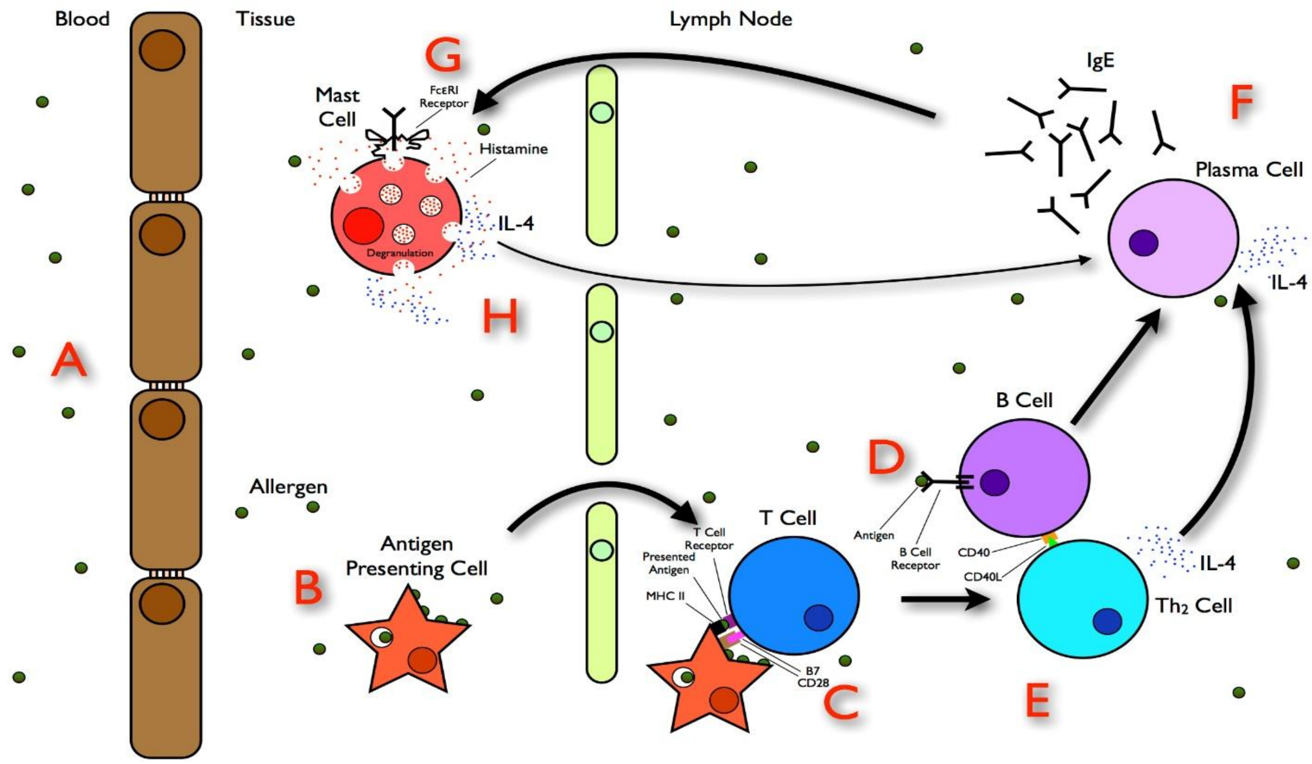

Figure 1. The IgE mediated allergy pathway (Sabban 2011). Abbreviations: B Cell – B lymphocyte. B7 – Receptor protein. CD28, CD40, CD40L – T Cell antigens. FcεRI receptor – High-affinity IgE Fc receptor. IgE – Immunoglobulin E. IL-4 – Interleukin 4. MHC II – Mega histocompatibility complex II. T Cell – T lymphocyte. Th1 Cell – T helper cell type 1. Th2 Cell – T helper cell type 2.

There is no single laboratory test at the moment to diagnose allergies and therefore diagnosis, especially concerning food allergies, is done by controlled elimination – challenge procedures. The IgE measurements of the blood are a valid predictive tool, but do not serve solely when diagnosing clinical allergy (Tricon et al. 2006).

Reasons and mechanisms that lead to the development of allergic reactions are still unclear on most parts although, the pathway for allergic reaction is well known. Some allergic reactions are caused by non-IgE mediated mechanisms, such as delayed immune reactions which are cell mediated. This study concentrates solely on the IgE mediated reactions.

2.4 The relevance of early life diet in the development of allergic diseases in childhood

The current hypothesis is that changes in dietary intake may be one of the main reasons for the major increase in allergy prevalence (Seaton et al. 1994, Black and Sharpe 1997, Fogarty and Britton 2000). Early life diet has been associated with asthma and allergies in epidemiological studies (Table 3). However, the conclusion in several review articles has been, that the results of the studies are somewhat inconclusive and inconsistent (Devereux 2006, Devereux and Seaton 2005, Heine and Tang 2008). Although studies of food consumption in relation to allergy development have not been able to conclude anything consistent, the trend seems to be that mostly positive effects can be achieved with food consumption.

Table 3. Summary of evidence from epidemiological studies assessing the role of early life diet in relation to allergic outcomes.

Reference, country	Study design	Length of follow up	Subjects	Dietary assessment method	Outcomes and assessment	Main findings
Nafstad et al. 2003, Norway	Prospective birth cohort	4 years	2531 new-born infants	Parental questionnaires at birth and when the children were ½, 1, 1½, 2, and 4 years old	Doctor diagnosed asthma and allergic rhinitis.	Early introduction of fish in the diet was negatively associated with the risk of allergic rhinitis.
Kull et al. 2006, Sweden	Prospective birth cohort	4 years	4089 new-born infants	Parental questionnaires at ages 2 months, 1, 2 and 4 years	Blood sampling for analysis of specific IgE to common food and airborne allergens.	Regular fish consumption during the first year of life was associated with a reduced risk of allergic disease by age 4.
Waser et al. 2007, Switzerland	Cross-sectional	No follow up	14 893 children, 5-13 years of age	A detailed parental questionnaire	Allergen-specific IgE was measured in serum.	Consumption of farm milk may offer protection against asthma and allergy.
Nagel et al. 2010, Germany	Cross-sectional	No follow up	63 000 school children, 8-12 years of age	Parental questionnaires	Parental questionnaires, skin prick testing.	Diet is associated with wheeze and asthma but not with allergic sensitization. 'Mediterranean diet' may provide some protection against wheeze and asthma in childhood.
Nwaru et al. 2010, Finland	Prospective birth cohort	5 years	994 new-born infants	Age-specific dietary questionnaires, with a follow-up form on the age at the introduction of new foods	Specific IgE concentration measurements	Late introduction of solid foods was associated with increased risk of allergic sensitization to food and inhalant allergens.
Virtanen et al. 2010, Finland	Prospective birth cohort	5 years	1293 new-born infants	Parental record on the age at introduction of new foods	International Study of Asthma and Allergies in Childhood-type questionnaire	Early introduction of oats was associated with decreased risk of persistent asthma and early introduction of fish for the decreased risk of allergic rhinitis.

(continues)

Table 3, continues

Reference, country	Study design	Length of follow up	Subjects	Dietary assessment method	Outcomes and assessment	Main findings
Loss et al. 2011, Switzerland	Cross-sectional	No follow up	8334, 6-12 year old children	Parental questionnaire	Specific IgE measurements, questionnaire of clinical outcomes using International Study of Asthma and Allergies in Childhood standards	Reported raw milk consumption was inversely associated to asthma.
Rosenlund et al. 2011, Sweden	Cross-sectional	No follow up	2447, 8 year old children	Parental questionnaires at 8 years of age	Allergen-specific IgE levels from blood samples	An inverse relation was observed between total fruit consumption and rhinitis.
Nwaru 2012, Finland	Prospective birth cohort	5 years	994 new-born infants	Parental record on the age at introduction of new foods	Allergen specific IgE measurement	Sensitization to wheat allergen was associated with late introduction of potatoes, wheat, rye, fish, and eggs. The risk of sensitization to any inhalant allergen increased with late introduction of potatoes, rye, meat, and fish.
Magnusson et al. 2013, Sweden	Prospective birth cohort	12 years	3285 new-born infants	Parental questionnaires	Allergen specific IgE measurements and parental questionnaires of allergic symptoms	Regular fish consumption in infancy may reduce the risk of allergic disease up to 12 years of age.
Nwaru et al. 2014, Finland	Prospective birth cohort	5 years	3142 new born infants	Food records at the ages of 3, 4, 6 and 12 months	International Study of Asthma and Allergies in Childhood questionnaire	Less food diversity during the first year of life might increase the risk of asthma and allergies in childhood.
Roduit et al. 2014, Austria, Finland France, Germany and Switzerland	Prospective birth cohort	6 years	856 new born infants from rural areas	Monthly food records during the first year of life	Parental questionnaire	An increased diversity of complementary foods introduced in the first year of life was inversely associated with asthma, food allergy and food sensitization.

The most common food items studied are fish, fruit and vegetables. In addition to food items other nutritional factors, such as vitamins and fatty acids, have been studied widely. Few studies have also been conducted with the Mediterranean diet (Chatzi and Kogevinas 2009, Nurmatov et al. 2011).

Prospective birth cohort study (PASTURE/EFRAIM) involving children from five European countries (Austria, Finland, France, Germany and Switzerland) concluded that increased diversity of complementary foods introduced in the first year of child's life lowered the risk of developing allergic diseases (Roduit et al. 2014). These results strengthen the increasing assumption that exposure to different food allergens in infancy and early childhood might reduce the risk of allergic diseases rather than increase it. In the International Study on Allergies and Asthma in Childhood (ISAAC) Nagel et al. (2010) concluded that diet is associated with asthma and wheeze but not with allergic sensitization. However, diet and allergic sensitization have been associated repeatedly in studies investigating the introduction of complementary feeding (Nafstad et al. 2003, Virtanen et al. 2010, Nwaru 2012, Longo et al. 2013).

Overall, the conclusion in most studies seems to be that diet most likely influences the development of allergic diseases (Devereux and Seaton 2005, Nagel et al. 2010, Lepski and Brockmeyer 2013). There are strong indications that diet could in most cases decrease the prevalence of asthma and allergies, though the relation and the mechanisms are still partly unclear (Sala-Vila et al. 2008, Oien et al. 2010). It is evident that more studies investigating the association of allergic diseases and different dietary factors, early feeding practice and maternal diet are needed to make further conclusion and future recommendations.

2.5 Early life exposure as part of the mechanism in atopic sensitization

The associations between maternal consumption of foods, breastfeeding as well as early feeding practices and allergies, might explain the mechanisms behind the development of atopic sensitization later in child's life. Even when studying food consumption of the child, the possibility needs to be considered, that the exposure during pregnancy and breastfeeding might affect the atopic sensitization of the child alongside with food consumption, since the sensitization might already develop during the gestation and/or breastfeeding (Palmer and Prescott 2012).

The implications that maternal consumption of foods and breastfeeding potentially play an important role in the immunological development of the child are strong (Longo et al. 2013). A meta-analysis from 2001 concluded that exclusive breastfeeding for the first 3 months was protective against atopic dermatitis (Dattner 2010). However Dattner (2010) points out that opposite association was found in a Danish study (Host et al. 1988) where exclusive breastfeeding for the first four months increased the risk of atopic dermatitis for children with the family history of allergy. A similar conclusion was found in a Finnish study from 2006, where prolonged exclusive breastfeeding was found to increase the risk of atopic dermatitis and food hypersensitivity for children with family history of allergy (Pesonen et al. 2006). However, this might also be a result from delayed introduction of solid foods (Nwaru et al. 2010, Nwaru 2012) and not the breastfeeding itself. It seems that the protective effect of breastfeeding is highly modified by maternal allergy (Heine and Tang 2008).

Erkkola et al. (2012) concluded that maternal diet during pregnancy may influence the development of allergic diseases later in childhood. The researchers assessed data from 2441 Finnish children at 5 years of age. In another Finnish study, high maternal consumption of cow’s milk and cow’s milk products were associated with a decreased risk of cow’s milk allergy in the offspring (Tuokkola 2011). The association was found even stronger if the mother of the child had no allergy. The researchers conclude that their findings strengthen the evidence of the impact that maternal diet might have on the disease development later in child’s life.

In addition to cow’s milk, increased intake of oily fish during pregnancy has found to be effective in reducing the incidence of asthma at 2 years of age (Dotterud et al. 2013). No significant change was found for wheeze and atopic dermatitis (eczema). Similar results were found in a Danish national birth cohort study were high maternal fish consumption during pregnancy was found protective against asthma up to seven years of age (Maslova et al. 2013). Maternal intake of fatty acids during pregnancy has also been associated with childhood asthma, although, in this study the researchers did not found any association between asthma and maternal intake of oils, fish and fish products (Lumia et al. 2011). In addition, maternal intake of butter and saturated fatty acids during lactation have been associated with increased risk of allergic sensitization of the child, while margarine and low fat spreads have found to decrease the risk of sensitization to allergens (Nwaru et al. 2011).

Although the results from the studies concerning breastfeeding and maternal diet are mainly pointing in the same direction, there are still some contradictions in the evidence. Especially the role of breastfeeding is highly controversial and difficult to study since it cannot be controlled. The introduction of solid foods seems to confound it even more. Exclusive breastfeeding might lead to the delayed introduction of solid foods that might cause the critical window (see chapter 2.5.1) to close before exposal to food allergens occurs. The evidence is not clear on how much allergen exposure is received via breast milk and whether this might be enough to change the immunological development of the child.

There do not seem to be any reliable data supporting the positive effect of any restrictions in the maternal diet during pregnancy or lactation, even with high risk infants. At the moment, the WHO guideline recommends exclusive breastfeeding for the first 6 months. This is in contrast with the data supporting early introduction (< 6 months) of allergenic foods for high risk infants (Longo et al. 2013). The recommendation for exclusive breastfeeding in Finland at the moment is the same as the WHO guideline (Hasunen et al. 2004).

2.5.1 The critical window

The term “critical (or crucial) window” is used to describe a time period where the child should be exposed to certain food proteins or the risk of developing allergic diseases increases. It has been suggested that because most food allergies seem to develop during the first year of life it might indicate that there is a critical time period in the early life for the development of food allergies (Hong and Wang 2012).

The immunological processes in the infant’s intestine support the theory of the critical window. The infant’s intestinal colonization develops in the first few months of the child’s life and changes in the colonization pattern might affect the immune responses of the intestine (Molloy et al. 2013). To support the critical window hypotheses, children who develop allergy by the age of 5 years have been found to have higher Th2 cytokine responses at the age of 1 year (Holt et al. 2010).

The critical window for tolerance development is mentioned in several studies investigating the role of diet, breastfeeding or timing of the introduction to solid foods in the development of allergic diseases (Hong and Wang 2012, Nwaru 2012, Longo et al. 2013). It is suggested to be especially important if the child is considered as a high risk infant with a genetic susceptibility to atopic sensitization.

2.6 Specific foods and allergic sensitization

2.6.1 Dietary fat – quality or quantity

The lipid hypothesis, which is one of the main dietary hypotheses in the study of allergic diseases, focuses on long-chain polyunsaturated fatty acids (PUFA) in the diet (Devereux 2006, Sala-Vila et al. 2008, Torres-Borrego et al. 2012). The hypothesis proposes that the increased prevalence of asthma and allergic diseases is partly caused by the increased intake of n-6 PUFA and decreased intake of n-3 PUFA (Devereux and Seaton 2005, Klemens et al. 2011). It also suggests that too much n-6 PUFA in relation to n-3 PUFA alters the lipid composition of the membranes of inflammatory cells, causing certain type of pro-inflammatory reaction. N-6 PUFA acts as a direct precursor of inflammatory eicosanoids leukotriene B4 (LTB4) and prostaglandin E2 (PGE2) (Klemens et al. 2011). These eicosanoids can promote Th2 differentiation and therefore IgE production (Figure 1.). In contrast n-3 PUFA promotes less inflammatory eicosanoids (LTB5 and PGE3) with inflammation lowering potential (D'Vaz et al. 2012).

There are indications of a beneficial association between high n-3 PUFA intake and hay fever, atopic disease and asthma in children, but also some contradicting evidence that n-3 PUFA intake might increase the risk of asthma (Devereux and Seaton 2005, Devereux 2006, Klemens et al. 2011). In a cross sectional study of Finnish children's nutritional data collected in 1980, margarine use compared with butter use was associated with decreased risk of atopic disease (Dunder et al. 2001). Differences in serum fatty acid composition measured from the children supported the findings from the nutritional data. These findings are in line with the general opinion associating polyunsaturated fatty acids for the decreased risk of atopic sensitization. Sala-Vila et al. (2008) conclude in their review, that even though there are strong indications that there is a link between measurements of fatty acid composition in blood and allergic diseases, there is no clear evidence of which particular fatty acids or groups of certain type of fatty acids are in play.

In addition to dietary fatty acids, supplementation of n-3 PUFA has been studied widely. However, it has not been found effective in preventing allergy, even though the plasma levels of polyunsaturated fatty acids were elevated among infants receiving n-3 PUFA as supplements (D'Vaz et al. 2012). In a systematic review (Kremmyda et al. 2011) the researchers came to conclusion that fish oil supplementation in infancy might lower the risk of some allergic conditions but the results are mainly contradicting. In an Australian study, Palmer et al. (2012) found that maternal fish oil supplementation during pregnancy lowered the incidence of atopic eczema and egg sensitization, but did not reduce the overall sensitization to IgE mediated allergies.

In a Finnish study assessing the role of breast milk composition in the development of atopic dermatitis Hoppu et al. (2005) concluded that breast milk low in n-3 PUFA and high in saturated fatty acids, may increase the risk of atopic dermatitis in high risk infants. In another Finnish study investigating the role of breastfeeding in the development of atopic sensitization of the child, maternal diet rich in saturated fat during pregnancy was associated with increased risk of atopic sensitization (Hoppu et al. 2000). Nevertheless, the researchers mention that the high intake of saturated fat in the mother's diet might also indicate otherwise poor diet and might not be the only dietary factor contributing to the outcome. Although these studies are observing breastfeeding, the results show the possible connection between dietary fatty acid composition and atopic sensitization.

The common opinion at the moment seems to be that even though the results are fairly inconclusive and somewhat conflicting, the imbalance between n-6 PUFA and n-3 PUFA intake could be partly to blame for the increased prevalence of asthma and allergic diseases (Devereux and Seaton 2005). Nevertheless, the optimal ratio of n-6 PUFA and n-3 PUFA for health benefits is still under investigation. Although it is clear that more studies investigating dietary fat intake are needed, studies of individual fatty acids provide useful information on how different dietary fats might associate with the development of allergic diseases.

2.6.2 Fish consumption

Number of studies suggest that fish consumption in early childhood is associated with a lower risk of developing allergies or asthma later in child's life (Nafstad et al. 2003, Kull et al. 2006, Oien et al. 2010, Dotterud et al. 2013, Magnusson et al. 2013). The beneficial associations found with fish consumption are suggested to be due to the polyunsaturated fatty acids, Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA), in fish, which have protective effect against inflammation, the mechanisms of which are explained in the previous chapter (2.6.1) (Nafstad et al. 2003).

However, it seems that fish oils independently as a supplement might not be as effective as dietary fish. A Norwegian study (Oien et al. 2010) investigating the different associations which fish oil supplementation and fish consumption might have in the development of asthma and eczema, found that in the prevention of eczema, dietary fish was more effective than fish oil supplementation or the total intake of n-3 PUFA. D'Vaz et al (2012) add, that the poor results of fish oil supplementation applies even when it has improved the n-3 PUFA status of the child. These findings suggest that there are some other components in fish in addition to fatty acids that influence the outcome, or that fish consumption might possibly be a reflection of other dietary habits (Nafstad et al. 2003). Oien et al. (2010) also conclude that fish consumption during infancy seems to be more important than maternal intake during pregnancy, at least considering eczema prevention in childhood. These findings are also supported in the clinical practice guideline for allergy prevention (Muche-Borowski et al. 2009), which recommends that fish is given as solid food for infants.

In a prospective birth cohort study that followed 4089 new-born infants for four years, researchers found a connection between regular fish consumption during the first year of life and reduced risk for eczema, allergic rhinitis and sensitization by the age of four (Kull et al. 2006). Reduced risk was found among children who consumed fish at least twice a month. In a Norwegian study, a reduced risk of developing eczema was found with children who ate fish once a week or more (Oien et al. 2010). Supporting the possible profitable effects of fish consumption Dotterud et al. (2013) found that increased intake of oily fish during early childhood may be protective against asthma at 2 years of age. In addition, in a Swedish prospective birth cohort study the researchers found that fish consumption in infancy might decrease the risk of allergic disease, particularly allergic rhinitis and eczema, up to 12 years of age (Magnusson et al. 2013).

There is some evidence that fish consumption may only apply to some allergens and it seems that the profitable effect of fish comes from regular consumption. The amount and frequency of fish consumption and the type of fish (oily or lean) probably have an important role in the outcome as well (Andreasyan et al. 2005). The age of the introduction also seems to be important, and it seems that especially children who are genetically at risk and might benefit the most, are introduced to fish later in life (Kull et al. 2006). The sensitization for fish itself seems to be rare, even if fish is introduced at early age. Some researchers speculate that fish consumption might reflect other dietary and lifestyle factors which make it difficult to separate the effects (Nafstad et al. 2003, Magnusson et al. 2013).

In conclusion, there is evidence that fish consumption in early life might reduce the risk of at least some allergic conditions. However, as for other dietary factors, the evidence is not conclusive and needs further exploring.

2.6.3 Unprocessed cow’s milk and egg consumption

Studies investigating cow’s milk, hen’s egg and cereals in relation to allergies are rare. The studies conducted with cow’s milk consumption has mainly showed profitable results for raw milk consumption and the evidence from studies assessing egg consumption has not been conclusive. Terms “raw milk”, ”farm milk” or “unprocessed milk” all stand for cow’s milk which has not been pasteurized or otherwise heat treated and is usually acquired directly from a farm. The results from the studies assessing raw milk consumption, show some promising evidence of reducing the risk of asthma, allergic rhinitis and sensitization to some allergens (Waser et al. 2007, Braun-Fahrländer and von Mutius 2011, Loss et al. 2011). However, some researchers speculate that the association found with the reduced risk of asthma could be at least to some extend due to the fact that parents have stopped feeding their children milk after asthma diagnosis, since cow's milk has been proposed to influence further asthma development (Fussman et al. 2007).

In a study investigating the role of farm products in asthma and allergy development, Waser et al. (2007) found an inverse association with farm milk consumption and allergic rhinitis, sensitization to pollen and food allergens with children 5-13 years of age. Researchers do not mention whether the inverse association they observed, could be due to dietary modification caused by asthma diagnosis, as Fussman et al. (2007) suggested. The researchers conclude that the results could not be explained by other farm exposures (e.g. other dietary factors or contact with farm animals) during pregnancy or childhood. In this study, researchers also found that egg consumption might reduce the risk of asthma and allergic rhinitis, but after adjustment only the association of farm milk consumption was statistically significant. In a review assessing farm milk consumption and allergies, Braun-Fahrländer and von Mutius (2011) also conclude that there is strong evidence that unprocessed milk may reduce the risk of asthma, hay fever as well as atopic sensitization.

The results of a double blind, randomized controlled trial by Palmer et al. (2013) showed increased immune tolerance and reduced risk in egg allergy development for high-risk infants who had regular egg consumption at early age (≥ 4 months). However, in this study the researchers point out that although high-risk infants might benefit from early egg exposure it must be executed with caution since some infants may have sensitized to egg already by the age of 4 months.

The mechanisms by which cow's milk might affect the immunological processes in allergy development are considered to be the specific components in milk that may weaken the atopic sensitization. These components have been suggested to be able to affect the maturation of regulatory T (Treg) cells and, in addition, they have considered to be able to suppress cytokine (IL-4) synthesis and prevent Th2-mediated IgE production (described in Chapter 2.3) (Melnik et al. 2014). It is speculated, that one of the reasons why results with unprocessed milk consumption are more significant than with processed milk, is that some of these compounds are being destroyed by heat. Some studies have included the information of whether the unprocessed milk has been heated at home previous to consumption (Loss et al. 2011), but the possible relevance of this is unclear.

In conclusion, the mechanisms in which cow's milk is related to asthma and allergies are still largely unclear and as Braun-Fahrländer and von Mutius (2011) mention in their review, there is no certain knowledge of which components in milk might be relevant. Moreover, since there are potential pathogens in the unprocessed cow's milk, it cannot be recommended for the prevention of allergic diseases.

2.6.4 Fruit and vegetables

Fruit and vegetable consumption have been suggested to reduce the risk of allergic diseases (Rosenlund et al. 2011). This is due to the fact that they contain a high amount of vitamins and antioxidants which are suspected to play a part in the immunological process of allergy development. Vitamins and antioxidants may contribute to Th1/Th2 balance or down regulate Th2 responses and therefore may reduce the risk of atopic diseases or lead to reduced IgE production (Andreasyan et al. 2004, Hong and Wang 2012).

The beneficial association of fruit and vegetable consumption on the decreased incidence of asthma and allergies has been shown in some epidemiological studies (Lepski and Brockmeyer 2013). Rosenlund et al. (2011) found an inverse association between total fruit intake and allergic rhinitis at the age of 8 years. The inverse association was strongest between the consumption of apples, pears and carrots and allergic rhinitis, asthma and atopic sensitization. In this study, the fruit and vegetable consumption data were collected from the past year. However, the researchers conclude that these associations might be partly caused by disease-related diet modification, since after excluding children with previous allergic symptoms, the results were no longer statistically significant.

Studies investigating fruit and vegetable consumption are also rare. Studies investigating individual nutrients have been conducted more extensively. The available epidemiologic evidence in relation to fruit and vegetable consumption and allergy is limited and weak. Some supportive evidence is available regarding certain vitamins and the Mediterranean diet (Nurmatov et al. 2011) which could indicate the relevance of fruit and vegetable consumption.

Although, results from studies with individual vitamins and antioxidants are likely to explain the beneficial effects of fruit and vegetables in the diet, they should be studied along with actual food consumption to better understand the complete picture.

3 MATERIALS AND METHODS

3.1 Subjects and study design

The current study is based on the Type 1 Diabetes Prediction and Prevention (DIPP) Nutrition study. DIPP Nutrition study is a part of the larger DIPP study. The DIPP study is a prospective population based birth cohort study, which started in 1994 and aims to predict and prevent type 1 diabetes. All newborn infants in Tampere, Turku and Oulu University hospitals were screened for HLA-DQB1–conferred susceptibility to type 1 diabetes mellitus (DM). Infants with increased genetic susceptibility for type 1 DM were invited to participate in the DIPP study and have been monitored for diabetes-associated auto-antibodies, growth, and viral infections at 3–12-month intervals for 5 years in the current study (Virtanen et al. 2010, Lumia et al. 2012).

DIPP Nutrition study started in 1996 and involved children from Tampere and Oulu University Hospitals. The study aims to investigate the associations between diet during pregnancy, lactation, infancy, and early childhood and the development of type 1 diabetes, allergies and asthma and obesity in childhood (Virtanen et al. 2010).

At 5 years of age, children who were still participating in the dietary follow up, were invited to the DIPP Allergy Study (Virtanen et al. 2010, Lumia et al. 2012). The families completed a questionnaire modified from the ISAAC questionnaire on the child's history of allergic symptoms and allergic diseases (Nwaru 2012). Blood samples were taken for the measurement of IgE antibodies to specific food and inhalant allergens. The measurement of IgE antibodies is explained in detail in chapter 3.3. This study is based on a cohort design and the children included in this study are from Tampere area and constituted a total of 1928 children.

3.2 Dietary assessments

Information on the children's diet was collected by using a three-day food record at the age of 3 and 6 months and 1, 2, 3, 4 and 6 years. The families were instructed to include three consecutive days in the food records; two weekdays and one day of weekend. After returned by families, the records were checked by trained research nurses at the research clinics (Virtanen et al. 2012). For the collection of the dietary records of the children, the staff at the research clinics was regularly trained by the research nutritionists. In addition, each nurse or doctor received individual training. The following issues were emphasized especially: the aims of the study, importance of food-data collection; knowledge of food items on the market; the type of foods eaten; the place and type of preparation of food; the composition of foods and dishes (brand names and recipes); dietary supplements and foods enriched with nutrients; ability to check the amounts of foods and drinks and the necessary information in the recording. The research personnel were also informed about childhood nutrition overall and they were able to practice in checking of the food records.

The families were given advice by the trained research staff on how to complete the child's food records. Daycare personnel were given separate food record forms and families were asked to check the food records completed by the daycare personnel. Contact information was inquired from the daycare and recipes and menus were asked in detail. The families and day care personnel received written advice that included an example of a one day food record. They were also asked to fill in eating dates, times and places. Families were encouraged not to change anything on the child's diet during the food recording. For the estimation of the amounts of foods used, families and day care personnel received a booklet of portion sizes, household measures and food brochures. At study centers updated food product brochures and lists of dietary supplements were used to help identify the foods used. Annually updated national food database was also used. Intake of each food from different food items were able to be summarized using the national food database and connected software. Commercial baby foods were added to the food database by the DIPP Nutrition study group and they were updated annually.

The current study utilizes the food consumption data of the children up to the age of 3 years. The food record data will relate to each age point of the collection of food records to the study endpoints; 3 and 6 months and 1, 2 and 3 years of age. The food groups of interest in the current study include egg, fruit and berry juices, cereals (oat, barley, rye, wheat, rice, buckwheat, corn flour, millet), fish, fish products, shellfish, cow's milk products, vegetables, fruit, berries, potatoes, roots, meat and dietary fats.

3.3 IgE measurements

The IgE concentrations were analyzed from the children's blood samples at the age of 5 years by using ImmunoCAP fluoroenzyme immunoassay (Phadia Diagnostics, Uppsala, Sweden) (Nwaru et al. 2010). The measurements included the following food and inhalant allergens: egg, cow's milk, fish, wheat, house dust mite, cat, timothy grass, and birch. The IgE endpoints studied in the present study were: any food allergen (i.e. any of egg, cow's milk, fish or wheat allergen), any inhalant allergen (i.e. any of house dust mite, cat, timothy grass, or birch allergen), and any allergen (i.e. any food or inhalant allergen). Allergic sensitization for each endpoint was studied at the level ≥0.35 kU/l.

4 STATISTICAL ANALYSES

Simple descriptive statistical methods (Pearson's chi-square test) were used to examine the characteristics of the study population with regards to the endpoints and food consumption. Food consumption of the children were analyzed as means and standard deviations of intake in grams. The associations between food consumption and each endpoint were analyzed at each age of dietary assessment (3 and 6 months and 1, 2 and 3 years) using logistic regression and appropriate data analysis method, respectively. The unadjusted model was also adjusted for total energy intake. The results of the association between food consumption and IgE sensitization were adjusted for potential confounding variables such as child's sex, maternal and paternal educational level (none, vocational school or course, secondary vocational school, university studies), statistical grouping of home municipality (rural municipality, semi urban municipality, urban municipality), maternal smoking during pregnancy (no, yes), parental asthma or allergic rhinitis (no, yes), mode of delivery (vaginal, caesarian section), birth weight (< 2500, ≥ 2500 g), pets at home during the first year of life (no, yes), the number of siblings (0, 1, 2 or more), duration of total breastfeeding (< 5, 5-9.5, ≥ 10 months) and total energy intake.

Food consumption was regrouped at each age point as follows: food variables that were used by more than 5 % but less than 24 % of the study population were separated to two groups; non-users and users. Food variables which were used by 25 % or more or were not used by less than 5 % of the study population were divided in to quartiles. The food variables that had significantly low number of non-users or no non-users at all (all study subjects were using the food in question), the comparison was done to the first quartile (lowest intake of the food) instead of comparison to the non-users. Food variables that were used by less than 5 % of the study population were not analyzed. The food variables that were included in the final analysis are described in table 4. Statistical analysis was done by using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.

Table 4. The food variables included in the analysis at different age points.

Food variable	3 months[1]	6 months[1]	1 year[1]	2 years[1]	3 years[1]
Eggs	–	–	x	x	x
Fruit And Berry Juices	–	x	x	x	x
Oat and barley	–	x	x	x	x
Rye	–	x	x	x	x
Wheat	–	x	x	x	x
Other cereals	–	x	x	x	x
Fish	–	x	x	x	x
Fish products	–	–	–	x	x
Cow's milk products	x	x	x	x	x
Vegetables	–	x	x	x	x
Fish shellfish and fish products	–	x	x	x	x
Fruit and berries	x	x	x	x	x
Potatoes and roots	x	x	x	x	x
Meat	–	x	x	x	x
Dietary fats	–	x	x	x	x
Beverages and liquid milk products	x	x	x	x	x

[1] age at the time of the food data collection.
x The association between the food variable and atopic sensitization was analyzed at this age point.
– The association between the food variable and atopic sensitization was not analyzed at this age point due to the low number of users.

5 RESULTS

5.1 Background characteristics

Of the 1928 children included in the study 51.6 % were boys. The majority of the children (79.5 %) lived in urban municipality and more than half (51.8 %) had at least one sibling at the time of birth. Sixty one per cent of the children had at least one parent with asthma or allergic rhinitis. The distribution of the study population by background characteristics is presented in table 5.

Table 5. Distribution of the background characteristics of the subjects.

CHARACTERISTIC	Frequency n (%)
Sex	
Boys	995 (51.6)
Girls	933 (48.4)
Statistical grouping of home municipality	
Rural municipality	185 (9.6)
Semi urban municipality	207 (10.7)
Urban municipality	1533 (79.5)
Missing information	3 (0.2)
Maternal age	
< 25	255 (13.2)
25 - 29.9	683 (35.4)
30 - 34.9	604 (31.3)
≥ 35	386 (20.0)
Missing information	34 (1.8)
Maternal vocational Education	
None	95 (4.9)
Vocational school or course	548 (28.4)
Secondary vocational education	840 (43.6)
University studies or degree	438 (22.7)
Missing information	7 (0.4)
Paternal vocational education	
None	109 5.7)
Vocational school or course	812 (42.1)
Secondary vocational education	553 (28.7)
University studies or degree	405 (21.0)
Missing information	49 (2.5)
Maternal smoking	
No	1737 (90.1)
Yes	137 (7.1)
Missing information	54 (2.8)
Parental asthma or allergic rhinitis	
No	543 (28.2)
Yes	1184 (61.4)
No info	201 (10.4)
Mode of delivery	
Vaginal	1669 (86.6)
Caesarean section	256 (13.3)
Missing information	3 (0.2)

(continues)

Table 5, continues

CHARACTERISTIC	Frequency n (%)
Number of fetuses	
1	1836 (95.2)
2 or more	92 (4.8)
Birth weight	
<2500g	93 (4.8)
≥2500g	1832 (95.0)
Missing information	3 (0.2)
Number of siblings	
0	930 (48.2)
1	634 (32.9)
2 or more	364 (18.9)
Pet in house during first year of life	
No	1223 (63.4)
Yes	602 (31.2)
Missing information	103 (5.3)
Duration of total breastfeeding (months)	
< 5	604 (31.3)
5-9.5	673 (34.9)
≥ 10	612 (31.7)
Missing information	39 (2.0)
Duration of exclusive breastfeeding (months)	
< 0.7	668 (34.6)
0.7-3	624 (32.4)
≥ 3.2	610 (31.6)
Missing information	26 (1.3)
Total N	1928

The food consumption in the study population was diverse and age appropriate (in relation to national guidelines). Food consumption was not normally distributed and especially in the youngest user groups (3 and 6 months) the number of non-users were high. Shellfish and fish product consumption was so minimal that analysis of those groups individually was not possible. Shellfish and fish product consumption was included in the analysis of the fish/fish products/shellfish group.

5.2 Sensitization to allergens

Overall 37% of the children were sensitized to any allergen, 23% to any food allergen, and 26% to any inhalant allergen (Figure 2).

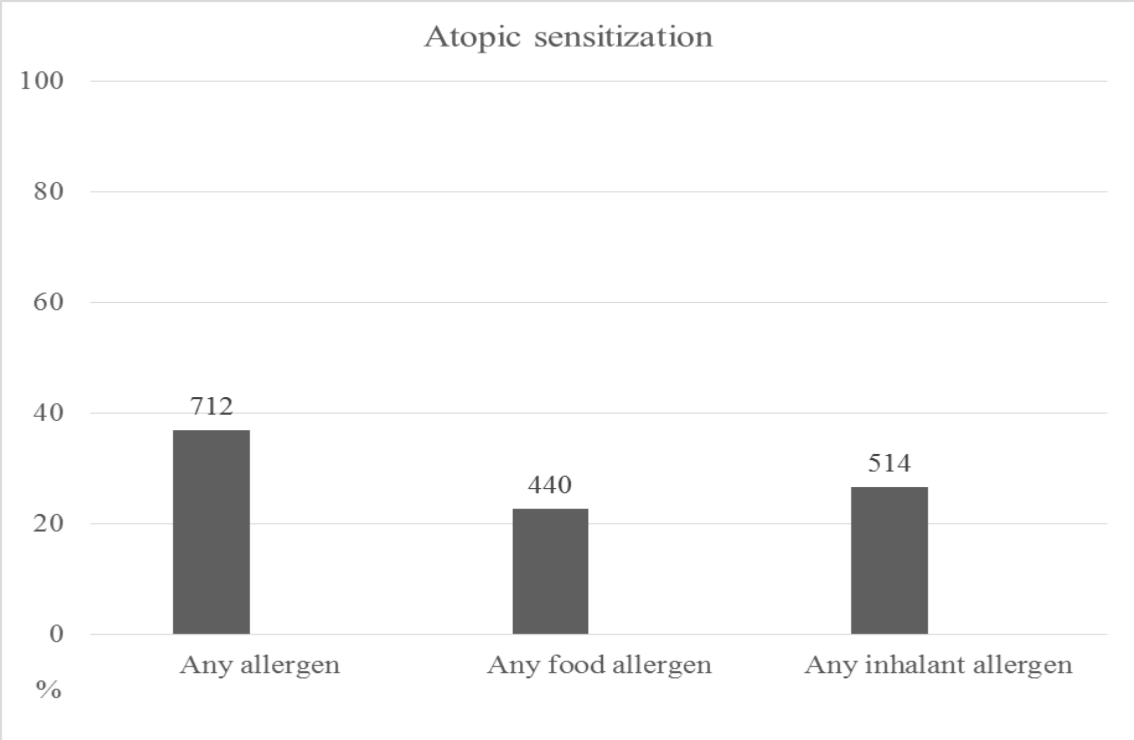

Figure 2. Sensitization to allergens in the study population.

5.2.1 Relation of background characteristics and allergic sensitization

The association between background characteristics and atopic sensitization is presented in table 6. Overall, most background characteristics were not associated with allergic sensitization in this study. Children with parental history of asthma or allergic rhinitis had higher prevalence of sensitization to any allergen, any food allergen, and any inhalant allergen. Children who lived in a house with a pet during the first year of life had a decreased risk of sensitization to any allergen and any food allergens and children who had had siblings had a decreased risk for the sensitization to inhalant allergens. A shorter duration of exclusive breastfeeding seemed also to decrease the risk of sensitization to inhalant allergens, although the duration of exclusive breastfeeding was not particularly long in this study population. Other factors were not statistically significantly associated with allergic sensitization.

Table 6. Distribution of atopic sensitization by background characteristics of the subjects.

CHARACTERISTIC	Any allergen IgE ≥0.35 kU/l n=712		Any food IgE ≥ 0.35 kU/l n=440		Any inhalant IgE ≥ 0.35 kU/l n=514	
	N (%)	p	N (%)	p	N (%)	p
Sex		0.142		0.649		0.105
Boys	383 (38.5)		223 (22.4)		281 (28.2)	
Girls	329 (35.3)		217 (23.3)		233 (25.0)	
Statistical grouping of home municipality		0.595		0.937		0.798
Rural municipality	71 (38.4)		43 (23.2)		48 (25.9)	
Semi urban municipality	82 (39.6)		49 (23.7)		59 (28.5)	
Urban municipality	557 (36.3)		347 (22.7)		405 (26.4)	
Maternal age		0.461		0.523		0.433
< 25	102 (40.0)		67 (26.3)		73 (28.6)	
25 - 29.9	260 (38.1)		156 (22.9)		189 (27.7)	
30 - 34.9	216 (35.8)		134 (22.2)		161 (26.7)	
≥ 35	134 (34.7)		83 (21.5)		91 (23.6)	
Maternal vocational Education		0.386		0.868		0.356
None	36 (37.9)		22 (23.4)		27 (28.4)	
Vocational school or course	187 (34.1)		118 (21.5)		130 (23.7)	
Secondary vocational education	325 (38.7)		197 (23.5)		234 (27.9)	
University studies or degree	160 (36.5)		100 (22.8)		119 (27.2)	
Paternal vocational education		0.481		0.406		0.345
None	43 (39.4)		25 (23.1)		34 (31.2)	
Vocational school or course	295 (36.3)		178 (21.9)		206 (25.4)	
Secondary vocational education	216 (39.1)		140 (25.3)		158 (28.6)	
University studies or degree	140 (34.6)		86 (21.2)		102 (25.2)	
Maternal smoking		0.956		0.685		0.905
No	638 (36.7)		392 (22.6)		461 (26.5)	
Yes	50 (36.5)		33 (24.1)		37 (27.0)	
Parental asthma or allergic rhinitis		**<0.01**		**<0.01**		**<0.01**
No	166 (30.6)		94 (17.3)		120 (22.1)	
Yes	479 (40.5)		304 (25.7)		351 (29.6)	
No info	201 (10,4)					
Mode of delivery		0.936		0.371		0.355
Vaginal	615 (36.8)		375 (22.5)		450 (27.0)	
Caesarean section	95 (37.1)		64 (25.0)		62 (24.2)	
Number of fetuses		0.662		0.308		0.722
1	680 (37.0)		423 (23.1)		488 (26.6)	
2 or more	32 (34.8)		17 (18.5)		26 (28.3)	
Birth weight		0.612		0.956		0.676
<2500g	32 (34.4)		21 (22.6)		23 (24.7)	
≥2500g	678 (37.0)		418 (22.8)		489 (26.7)	
Number of siblings		0.150		0.797		**0.044**
0	358 (38.5)		210 (22.6)		269 (28.9)	
1	235 (37.1)		150 (23.7)		164 (25.9)	
2 or more	119 (32.7)		80 (22.0)		81 (22.3)	
Pet in house during first year of life		**0.021**		**0.017**		0.136
No	474 (38.8)		296 (24.2)		343 (28.0)	
Yes	200 (33.2)		116 (19.3)		149 (24.8)	
Duration of total breastfeeding (months)		0.066		0.451		0.072
< 5	228 (37.7)		144 (23.8)		165 (27.3)	
5-9.5	267 (39.7)		158 (23.5)		196 (29.1)	
≥ 10	205 (33.5)		129 (21.1)		144 (23.5)	
Duration of exclusive breastfeeding (months)		0.122		0.513		**0.011**
< 0.7	228 (34.1)		142 (21.3)		165 (24.7)	
0.7-3	230 (36.9)		144 (23.1)		151 (24.2)	
≥ 3.2	242 (39.7)		146 (23.9)		189 (31.0)	

5.3 Associations between food consumption and allergic sensitization

5.3.1 The unadjusted associations

In the unadjusted model there was no association between food consumption at the age of 3 months and atopic sensitization (Table 7). At the age of 6 months inverse associations were seen for oat/barley, wheat and potatoes/roots in relation to all the endpoints. Inverse associations were also observed between rye consumption at the age of 6 months and any allergen and any inhalant allergen, as well as inverse associations between fruit/berry juices, fish and fish/shellfish/fish products and any inhalant allergen, beverages/liquid milk products and any food allergen and dietary fats and any allergen and any inhalant allergen. Consumption of other cereals (rice, buckwheat, corn flour and millet) were associated with increased risk of sensitization to any allergen (Table 8).

At the age of 1 year inverse associations were observed between oat/barley, rye, wheat, fish and fish/shellfish/fish products and all the endpoints. In addition, inverse associations were observed between egg and any food allergen and any inhalant allergen, vegetables and any allergen and potatoes/roots and any food allergen. An increased risk was observed for the consumption other cereals and all the endpoints (Table 9).

In the unadjusted model at the age of 2 years inverse associations were observed between egg and any allergen and any inhalant allergen, fruit/berry juices and any inhalant allergen, oat/barley and all the endpoints, wheat and any allergen and any food allergen, fish and fish/shellfish/fish products and any allergen and any inhalant allergen, and fruit/berries and any allergen and any food allergen. An increased risk was observed between other cereals and any allergen (Table 10).

At the age of 3 years the consumptions of egg, rye, wheat and cow’s milk products were associated with decreased risk of sensitization to all endpoints. Inverse associations were also found between fish and fish/shellfish/fish products and any inhalant allergen. Other cereals were associated with increased risk of atopic sensitization to any food allergen (Table 11).

5.3.2 The adjusted associations

At the age of 3 months, there was no association between food consumption and atopic sensitization in the adjusted model (Table 7). At the age of 6 months, inverse associations were seen for fruit/berry juices, oat/barley, rye, wheat, fruit/berries, potatoes/roots and dietary fats. The associations were strongest with oat/barley, wheat, and potatoes/roots, for which the inverse associations were observed for all endpoints. Consumption of fruit/berry juices and fruit/berries were associated with decreased risk of sensitization to any inhalant allergen, consumption of rye was associated with decreased risk of sensitization to any allergen and any inhalant allergen and consumption of dietary fats were associated with decreased risk of sensitization to any food and any inhalant allergen. At 6 months of age, consumption of other cereals (rice, buckwheat, corn flour and millet) were associated with increased risk of sensitization to any allergen (Table 8).

At the age of 1 year, inverse associations were seen for egg, oat/barley, rye, wheat, fish and fish/shellfish/fish products, vegetables and potatoes/roots. Consumption of egg, oat/barley, rye and wheat were found to decrease the risk of sensitization to all the endpoints. Consumption of potatoes/roots was associated with decreased risk of sensitization to any food and any inhalant allergen and the consumption of vegetables was associated with decreased risk of sensitization to any allergen. Consumption of other cereals (rice, buckwheat, corn flour and millet) at the age of 1 year, were found to increase the risk of sensitization to all allergens (Table 9).

In the adjusted model at the age of 2 years, inverse associations were seen for the consumption of egg, fruit/berry juices, oat/barley, wheat, fish and fish/shellfish/fish products and fruit/berries. Consumption of oat/barley and wheat were found to decrease the risk of sensitization to all the endpoints. Fruit/berry juices and fish/shellfish/fish products were inversely associated with sensitization to any allergen and any inhalant allergen as well as egg consumption was inversely associated with sensitization to any food and any inhalant allergen. Consumption of other cereals (rice, buckwheat, corn flour and millet) at the age of 2 years, were associated with increased risk of sensitization to any allergen and any food allergen (Table 10).

Consumption of egg, oat/barley, rye, wheat, fish, and cow’s milk at 3 years of age were inversely associated with atopic sensitization. Consumption of egg, rye, wheat and cow’s milk were found to decrease the risk of sensitization to all the endpoints. Consumption of fish and fish/shellfish/fish products were associated with decreased risk of sensitization to inhalant allergens (Table 11).

In the adjusted model, no associations were observed between consumption of meat or beverages/liquid milk products at any age point and atopic sensitization (Tables 7-11).

Table 7. Associations between food consumption at 3 months of age and atopic sensitization at 5 years of age.

Food variable g/day	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Cow's milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.19-163.33	0.92 (0.67-1.26)	0.83 (0.59-1.17)	0.72 (0.49-1.07)	0.67 (0.44-1.02)	0.91 (0.64-1.29)	0.84 (0.57-1.22)
Q 2: 164.63-600.83	1.02 (0.74-1.40)	0.85 (0.59-1.23)	0.94 (0.65-1.35)	0.75 (0.49-1.15)	1.06 (0.75-1.49)	0.83 (0.55-1.23)
Q 3: 601.46-833.33	0.76 (0.55-1.05)	0.58 (0.38-0.88)	0.74 (0.50-1.09)	0.52 (0.31-0.86)	0.74 (0.52-1.07)	0.57 (0.36-0.91)
Q 4: 836.08-1433.33	0.90 (0.65-1.24)	0.72 (0.48-1.10)	0.97 (0.68-1.40)	0.77 (0.47-1.25)	0.89 (0.63-1.27)	0.66 (0.42-1.05)
p-value	0.518	0.137	0.343	0.068	0.517	0.163
Fruit and berries						
Non-users	1	1	1	1	1	1
Users	0.79 (0.58-1.09)	0.701 (0.48-1.01)	1.03 (0.72-1.48)	0.99 (0.66-1.50)	0.79 (0.55-1.12)	0.70 (0.46-1.05)
p-value	0.155	0.059	0.855	0.969	0.186	0.082
Potatoes and roots						
Non-users	1	1	1	1	1	1
Users	1.04 (0.79-1.35)	1.00 (0.73-1.47)	1.18 (0.87-1.59)	1.25 (0.88-1.79)	0.93 (0.69-1.25)	0.85 (0.60-1.20)
p-value	0.801	0.994	0.291	0.211	0.638	0.357
Dietary fats						
Non-users	1	1	1	1	1	1
Users	1.05 (0.77-1.44)	1.02 (0.71-1.48)	1.11 (0.78-1.59)	1.06 (0.70-1.62)	1.09 (0.78-1.53)	1.09 (0.74-1.61)
p-value	0.761	0.901	0.563	0.778	0.621	0.674
Beverages and liquid milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.10-41.67	1.14 (0.85-1.53)	1.12 (0.81-1.53)	1.27 (0.92-1.76)	1.30 (0.91-1.85)	1.02 (0.74-1.41)	0.95 (0.67-1.35)
Q 2: 42.87-370.00	1.01 (0.75-1.35)	0.86 (0.61-1.19)	0.91 (0.64-1.28)	0.73 (0.49-1.09)	0.99 (0.71-1.36)	0.83 (0.58-1.19)
Q 3: 375.0-830.35	0.91 (0.68-1.23)	0.69 (0.47-1.01)	0.88 (0.62-1.26)	0.66 (0.42-1.03)	0.87 (0.63-1.21)	0.63 (0.41-0.96)
Q 4: 831.67-1602.44	0.89 (0.66-1.20)	0.73 (0.48-1.09)	0.97 (0.69-1.37)	0.78 (0.49-1.24)	0.88 (0.63-1.22)	0.66 (0.42-1.02)
p-value	0.688	0.197	0.430	0.052	0.870	0.210

[1] IgE ≥0.35 kU/l
[2] Adjusted for energy intake.
[3] Adjusted for energy intake, sex, maternal and paternal vocational education, statistical grouping of home municipality, maternal smoking, mode of delivery, pet in house during first year of life, birth weight, duration of total breastfeeding, number of siblings and parental asthma or allergic rhinitis.

Table 8. Associations between food consumption at 6 months of age and atopic sensitization at 5 years of age.

Food variable	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
g/day	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Fruit and berry juices						
Non-users	1	1	1	1	1	1
Users	0.80 (0.63-1.03)	0.78 (0.60-1.01)	0.82 (0.61-1.08)	0.82 (0.60-1.11)	0.75 (0.57-0.99)	0.69 (0.51-0.92)
p-value	0.078	0.058	0.160	0.193	**0.039**	**0.012**
Oat and barley						
Non-users	1	1	1	1	1	1
Q 1: 0.06-3.29	0.65 (0.48-0.86)	0.64 (0.47-0.87)	0.63 (0.45-0.88)	0.58 (0.41-0.83)	0.54 (0.39-0.74)	0.55 (0.39-0.77)
Q 2: 3.30-6.76	0.55 (0.41-0.74)	0.61 (0.45-0.84)	0.56 (0.40-0.79)	0.62 (0.43-0.90)	0.53 (0.39-0.73)	0.55 (0.39-0.77)
Q 3: 6.77-12.84	0.62 (0.47-0.83)	0.60 (0.44-0.83)	0.68 (0.48-0.94)	0.62 (0.43-0.89)	0.61 (0.45-0.83)	0.57 (0.40-0.80)
Q 4: 12.86-286.67	0.69 (0.52-0.92)	0.71 (0.52-0.97)	0.77 (0.56-1.07)	0.74 (0.52-1.05)	0.53 (0.39-0.74)	0.55 (0.39-0.77)
p-value	**< 0.01**	**0.003**	**0.005**	**0.010**	**< 0.01**	**< 0.01**
Rye						
Non-users	1	1	1	1	1	1
Q 1: 0.02-0.86	0.80 (0.54-1.19)	0.85 (0.56-1.29)	1.07 (0.70-1.65)	1.10 (0.69-1.74)	0.65 (0.41-1.02)	0.66 (0.41-1.07)
Q 2: 0.87-1.51	0.78 (0.52-1.15)	0.74 (0.48-1.13)	0.85 (0.54-1.35)	0.74 (0.44-1.23)	0.65 (0.41-1.02)	0.64 (0.39-1.04)
Q 3: 1.52-2.73	0.57 (0.37-0.86)	0.59 (0.38-0.92)	0.55 (0.33-0.92)	0.53 (0.30-0.92)	0.66 (0.42-1.03)	0.70 (0.44-1.13)
Q 4: 2.73-29.92	0.63 (0.42-0.95)	0.61 (0.39-0.96)	0.74 (0.46-1.20)	0.75 (0.44-1.26)	0.57 (0.35-0.91)	0.55 (0.33-0.92)
p-value	**0.013**	**0.031**	0.144	0.123	**0.010**	**0.026**
Wheat						
Non-users	1	1	1	1	1	1
Q 1: 0.02-1.35	0.69 (0.51-0.93)	0.69 (0.50-0.95)	0.69 (0.48-0.98)	0.64 (0.43-0.94)	0.64 (0.46-0.89)	0.62 (0.44-0.89)
Q 2: 1.36-3.52	0.56 (0.41-0.76)	0.55 (0.39-0.76)	0.56 (0.38-0.81)	0.57 (0.38-0.84)	0.58 (0.41-0.81)	0.54 (0.38-0.78)
Q 3: 3.54-7.77	0.73 (0.54-0.99)	0.72 (0.52-0.99)	0.80 (0.57-1.12)	0.75 (0.51-1.09)	0.59 (0.42-0.82)	0.57 (0.39-0.82)
Q 4: 7.80-50.00	0.74 (0.55-0.99)	0.69 (0.50-0.96)	0.76 (0.54-1.08)	0.71 (0.48-1.03)	0.52 (0.37-0.74)	0.49 (0.34-0.72)
p-value	**0.001**	**0.002**	**0.015**	**0.015**	**< 0.01**	**< 0.01**
Other cereals						
Non-users	1	1	1	1	1	1
Users	1.37 (1.05-1.78)	1.34 (1.01-1.78)	1.17 (0.87-1.59)	1.20 (0.87-1.65)	1.34 (1.01-1.78)	1.28 (095-1.73)
p-value	**0.020**	**0.042**	0.302	0.277	**0.040**	0.102
Fish						
Non-users	1	1	1	1	1	1
Users	0.81 (0.60-1.08)	0.81 (0.59-1.11)	0.75 (0.53-1.07)	0.80 (0.55-1.17)	0.71 (0.51-1.00)	0.70 (0.49-1.00)
p-value	0.152	0.191	0.118	0.256	**0.049**	0.050*
Cow's milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.33-129.31	0.87 (0.64-1.18)	0.99 (0.71-1.37)	0.74 (0.51-1.06)	0.82 (0.56-1.21)	0.84 (0.61-1.17)	0.89 (0.63-1.27)
Q 2: 129.53-501.67	0.87 (0.64-1.18)	0.92 (0.64-1.30)	0.99 (0.70-1.41)	1.05 (0.70-1.57)	0.72 (0.51-1.01)	0.68 (0.46-1.00)
Q 3: 504.68-692.74	1.15 (0.85-1.56)	1.24 (0.82-1.89)	1.04 (0.74-1.48)	1.10 (0.68-1.79)	1.06 (0.77-1.46)	0.90 (0.57-1.42)
Q 4: 693.23-1402.70	1.12 (0.83-1.51)	1.20 (0.78-1.84)	1.16 (0.83-1.64)	1.27 (0.77-2.07)	0.93 (0.67-1.29)	0.77 (0.48-1.24)
p-value	0.199	0.518	0.160	0.498	0.180	0.297

(continues)

Food variable g/day	Sensitization to any allergen[1] Unadjusted[2]	Sensitization to any allergen[1] Adjusted[3]	Sensitization to any food allergen[1] Unadjusted[2]	Sensitization to any food allergen[1] Adjusted[3]	Sensitization to any inhalant allergen[1] Unadjusted[2]	Sensitization to any inhalant allergen[1] Adjusted[3]
Vegetables						
Non-users	1	1	1	1	1	1
Q 1: 0.03-4.16	0.88 (0.65-1.19)	0.85 (0.61-1.18)	0.89 (0.63-1.26)	0.88 (0.60-1.28)	0.74 (0.53-1.04)	0.66 (0.46-0.96)
Q 2: 4.17-10.0	1.07 (0.79-1.43)	1.11 (0.81-1.54)	0.96 (0.69-1.35)	1.00 (0.69-1.45)	0.95 (0.68-1.31)	0.98 (0.69-1.38)
Q 3: 10.0-23.79	0.97 (0.72-1.31)	0.95 (0.69-1.32)	0.92 (0.65-1.30)	0.91 (0.63-1.33)	1.00 (0.73-1.39)	0.90 (0.64-1.28)
Q 4: 23.90-158.55	1.11 (0.82-1.49)	1.12 (0.81-1.54)	1.02 (0.72-1.43)	1.04 (0.72-1.50)	1.18 (0.86-1.62)	1.09 (0.77-1.54)
p-value	0.642	0.458	0.939	0.902	0.121	0.101
Fish, shellfish and fish products						
Non-users	1	1	1	1	1	1
Users	0.81 (0.60-1.08)	0.81 (0.59-1.11)	0.75 (0.53-1.07)	0.80 (0.55-1.17)	0.71 (0.51-1.00)	0.70 (0.49-1.00)
p-value	0.152	0.191	0.118	0.256	**0.049**	0.050*
Fruit and berries						
Non-users	1	1	1	1	1	1
Q 1: 0.29-25.65	0.61 (0.38-0.99)	0.62 (0.37-1.03)	0.82 (0.48-1.40)	0.87 (0.49-1.55)	0.51 (0.31-0.84)	0.48 (0.28-0.82)
Q 2: 25.87-45.82	0.59 (0.37-0.96)	0.57 (0.34-0.95)	0.70 (0.41-1.20)	0.69 (0.39-1.24)	0.54 (0.33-0.88)	0.48 (0.28-0.82)
Q 3: 45.83-66.92	0.63 (0.39-1.01)	0.60 (0.35-1.01)	0.80 (0.47-1.38)	0.82 (0.46-1.47)	0.47 (0.29-0.77)	0.41 (0.24-0.71)
Q 4: 67.04-237.72	0.60 (0.37-0.97)	0.56 (0.33-0.94)	0.74 (0.43-1.27)	0.70 (0.39-1.27)	0.49 (0.30-0.81)	0.42 (0.24-0.72)
p-value	0.296	0.264	0.685	0.514	0.051	**0.023**
Potatoes and roots						
Non-users	1	1	1	1	1	1
Q 1: 0.37-30.65	0.57 (0.34-0.93)	0.58 (0.34-0.99)	0.49 (0.29-0.83)	0.49 (0.27-0.85)	0.47 (0.28-0.78)	0.50 (0.29-0.85)
Q 2: 30.67-52.73	0.44 (0.27-0.73)	0.44 (0.26-0.76)	0.41 (0.24-0.71)	0.41 (0.23-0.72)	0.33 (0.20-0.54)	0.33 (0.19-0.57)
Q 3: 52.74-81.67	0.50 (0.30-0.83)	0.47 (0.28-0.80)	0.52 (0.31-0.89)	0.48 (0.27-0.84)	0.34 (0.20-0.56)	0.32 (0.19-0.56)
Q 4: 81.67-297.56	0.44 (0.27-0.73)	0.43 (0.25-0.73)	0.46 (0.27-0.78)	0.45 (0.26-0.79)	0.35 (0.21-0.59)	0.33 (0.19-0.57)
p-value	**0.010**	**0.01**	**0.025**	**0.042**	**< 0.01**	**< 0.01**
Meat products						
Non-users	1	1	1	1	1	1
Q 1: 0.29-8.36	1.05 (0.78-1.40)	0.96 (0.70-1.31)	0.95 (0.68-1.33)	0.89 (0.62-1.27)	0.94 (0.69-1.29)	0.87 (0.62-1.22)
Q 2: 8.36-14.75	1.02 (0.76-1.36)	0.99 (0.72-1.35)	1.07 (0.77-1.49)	1.05 (0.74-1.50)	0.83 (0.60-1.14)	0.80 (0.57-1.14)
Q 3: 14.77-21.44	0.88 (0.66-1.18)	0.87 (0.63-1.19)	0.67 (0.47-0.96)	0.62 (0.42-0.92)	0.93 (0.68-1.27)	0.90 (0.64-1.26)
Q 4: 21.44-150.13	1.10 (0.82-1.47)	1.03 (0.75-1.42)	1.14 (0.82-1.58)	1.05 (0.73-1.51)	0.83 (0.60-1.14)	0.77 (0.54-1.09)
p-value	0.729	0.879	0.075	0.073	0.725	0.612
Dietary fats						
Non-users	1	1	1	1	1	1
Q 1: 0.02-1.48	1.02 (0.75-1.38)	0.96 (0.70-1.33)	0.79 (0.56-1.12)	0.76 (0.52-1.09)	0.98 (0.71-1.36)	0.93 (0.66-1.31)
Q 2: 1.49-3.02	0.68 (0.50-0.93)	0.66 (0.47-0.92)	0.60 (0.42-0.85)	0.59 (0.40-0.87)	0.69 (0.49-0.97)	0.65 (0.45-0.93)
Q 3: 3.02-5.36	0.77 (0.56-1.05)	0.76 (0.54-1.07)	0.65 (0.46-0.93)	0.62 (0.42-0.92)	0.75 (0.53-1.04)	0.66 (0.45-0.96)
Q 4: 5.37-30.73	0.93 (0.68-1.26)	0.83 (0.59-1.17)	0.87 (0.62-1.22)	0.84 (0.57-1.23)	0.79 (0.57-1.10)	0.65 (0.45-0.94)
p-value	**0.041**	0.085	**0.030**	**0.042**	0.102	**0.038**

(continues)

Food variable g/day	Sensitization to any allergen[1] Unadjusted[2]	Sensitization to any allergen[1] Adjusted[3]	Sensitization to any food allergen[1] Unadjusted[2]	Sensitization to any food allergen[1] Adjusted[3]	Sensitization to any inhalant allergen[1] Unadjusted[2]	Sensitization to any inhalant allergen[1] Adjusted[3]
Beverages and liquid milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.33-238.13	0.37 (0.16-0.87)	0.41 (0.17-1.03)	0.42 (0.17-1.04)	0.46 (0.17-1.21)	0.39 (0.17-0.90)	0.40 (0.16-1.01)
Q 2: 238.29-558.59	0.48 (0.21-1.12)	0.49 (0.20-1.21)	0.62 (0.26-1.50)	0.63 (0.24-1.67)	0.35 (0.15-0.82)	0.33 (0.13-0.83)
Q 3: 560.89-934.11	0.46 (0.20-1.07)	0.43 (0.17-1.14)	0.51 (0.21-1.25)	0.47 (0.16-1.32)	0.43 (0.18-1.00)	0.35 (0.13-0.94)
Q 4: 934.80-1711.16	0.48 (0.21-1.12)	0.48 (0.18-1.29)	0.64 (0.26-1.54)	0.67 (0.23-1.93)	0.40 (0.17-0.92)	0.32 (0.12-0.88)
p-value	0.095	0.317	**0.047**	0.064	0.155	0.170

[1] IgE ≥0.35 kU/l
[2] Adjusted for energy intake.
[3] Adjusted for energy intake, sex, maternal and paternal vocational education, statistical grouping of home municipality,
maternal smoking, mode of delivery, pet in house during first year of life, birth weight, duration of total breastfeeding, number of siblings and parental asthma or allergic rhinitis.

Table 9. Associations between food consumption at 1 year of age and atopic sensitization at 5 years of age.

Food variable	Sensitization to any allergen[1]		Sensitization to any food allergen[1]		Sensitization to any inhalant allergen[1]	
g/day	Unadjusted[2]	Adjusted[3]	Unadjusted[2]	Adjusted[3]	Unadjusted[2]	Adjusted[3]
Egg						
Non-users	1	1	1	1	1	1
Q 1: 0.00 – 0.57	0.67 (0.49-0.91)	0.61 (0.43-0.85)	0.54 (0.37-0.79)	0.50 (0.33-0.77)	0.63 (0.45-0.89)	0.61 (0.42-0.88)
Q 2: 0.58 – 1.91	0.82 (0.61-1.11)	0.82 (0.59-1.14)	0.76 (0.54-1.08)	0.77 (0.53-1.12)	0.77 (0.56-1.07)	0.76 (0.53-1.08)
Q 3 :1.92 – 5.31	0.80 (0.59-1.08)	0.79 (0.58-1.09)	0.69 (0.48-0.98)	0.71 (0.48-1.03)	0.73 (0.52-1.01)	0.70 (0.49-0.99)
Q 4: 5.35 – 51.72	0.79 (0.58-1.07)	0.76 (0.55-1.05)	0.78 (0.55-1.10)	0.76 (0.52-1.11)	0.80 (0.58-1.11)	0.77 (0.54-1.09)
p-value	0.078	**0.040**	**0.010**	**0.015**	**0.049**	**0.036**
Fruit and berry juices						
Non-users	1	1	1	1	1	1
Q 1: 0.03 – 1.06	1.03 (0.75-1.41)	1.02 (0.73-1.43)	0.91 (0.63-1.32)	0.92 (0.62-1.36)	0.84 (0.59-1.20)	0.82 (0.57-1.19)
Q 2: 1.06 – 4.54	0.86 (0.62-1.19)	0.89 (0.63-1.26)	0.69 (0.46-1.02)	0.69 (0.44-1.06)	0.79 (0.55-1.13)	0.80 (0.55-1.17)
Q 3: 4.57 – 16.20	0.98 (0.72-1.35)	0.99 (0.70-1.38)	0.99 (0.69-1.42)	1.00 (0.69-1.47)	0.88 (0.62-1.25)	0.90 (0.62-1.29)
Q 4: 16.25 – 314.0	0.68 (0.49-0.96)	0.68 (0.47-0.99)	0.68 (0.45-1.01)	0.76 (0.49-1.17)	0.66 (0.46-0.97)	0.63 (0.41-0.95)
p-value	0.219	0.338	0.168	0.387	0.207	0.201
Oat and barley						
Non-users	1	1	1	1	1	1
Q 1: 0.0 – 8.88	0.40 (0.28-0.56)	0.41 (0.28-0.60)	0.39 (0.27-0.58)	0.40 (0.27-0.61)	0.34 (0.23-0.49)	0.34 (0.23-0.51)
Q 2: 8.88 – 16.30	0.43 (0.30-0.61)	0.46 (0.32-0.67)	0.39 (0.26-0.57)	0.40 (0.26-0.61)	0.41 (0.29-0.59)	0.42 (0.29-0.62)
Q 3: 16.32 – 28.10	0.45 (0.31-0.63)	0.43 (0.30-0.63)	0.48 (0.33-0.70)	0.45 (0.30-0.67)	0.43 (0.30-0.61)	0.43 (0.29-0.63)
Q 4: 28.19 – 542.8	0.46 (0.32-0.65)	0.47 (0.33-0.69)	0.60 (0.42-0.87)	0.61 (0.41-0.90)	0.33 (0.23-0.48)	0.33 (0.23-0.50)
p-value	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**
Rye						
Non-users	1	1	1	1	1	1
Q 1: 0.01 – 1.82	0.53 (0.39-0.71)	0.52 (0.38-0.72)	0.41 (0.28-0.58)	0.41 (0.28-0.60)	0.56 (0.41-0.77)	0.54 (0.39-0.76)
Q 2: 1.82 – 4.18	0.50 (0.37-0.67)	0.48 (0.35-0.66)	0.53 (0.38-0.74)	0.49 (0.34-0.71)	0.43 (0.31-0.60)	0.44 (0.31-0.62)
Q 3: 4.20 – 8.98	0.46 (0.34-0.62)	0.41 (0.30-0.57)	0.47 (0.33-0.66)	0.44 (0.30-0.63)	0.47 (0.34-0.64)	0.43 (0.30-0.61)
Q 4: 9.00 – 55.90	0.53 (0.39-0.71)	0.52 (0.38-0.71)	0.58 (0.42-0.81)	0.57 (0.40-0.82)	0.51 (0.37-0.70)	0.53 (0.38-0.74)
p-value	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**
Wheat						
Non-users	1	1	1	1	1	1
Q 1: 0.03 – 6.90	0.33 (0.22-0.50)	0.34 (0.21-0.53)	0.39 (0.26-0.60)	0.36 (0.23-0.57)	0.37 (0.24-0.56)	0.38 (0.24-0.59)
Q 2: 6.94 – 13.16	0.29 (0.19-0.45)	0.27 (0.17-0.43)	0.32 (0.21-0.49)	0.31 (0.19-0.49)	0.31 (0.21-0.48)	0.29 (0.19-0.46)
Q 3: 13.16 – 23.13	0.29 (0.19-0.45)	0.27 (0.17-0.42)	0.31 (0.20-0.47)	0.29 (0.18-0.46)	0.32 (0.21-0.49)	0.29 (0.19-0.46)
Q 4: 23.15 – 88.89	0.30 (0.20-0.46)	0.29 (0.18-0.46)	0.34 (0.22-0.53)	0.32 (0.20-0.51)	0.28 (0.19-0.43)	0.28 (0.18-0.45)
p-value	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**	**< 0.01**

(continues)

Table 9, continues

Food variable g/day	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Other cereals						
Non-users	1	1	1	1	1	1
Q 1: 0.03 – 0.59	0.78 (0.52-1.18)	0.75 (0.48-1.18)	0.81 (0.50-1.31)	0.80 (0.47-1.37)	0.88 (0.56-1.37)	0.86 (0.52-1.40)
Q 2: 0.59 – 1.42	1.05 (0.71-1.55)	1.09 (0.72-1.65)	0.59 (0.34-1.00)	0.59 (0.34-1.03)	1.23 (0.81-1.87)	1.32 (0.86-2.03)
Q 3: 1.42 – 3.53	0.68 (0.45-1.04)	0.68 (0.44-1.05)	0.84 (0.52-1.35)	0.85 (0.52-1.40)	0.78 (0.50-1.24)	0.76 (0.47-1.23)
Q 4: 3.71 – 85.75	2.18 (1.49-3.21)	2.11 (1.40-3.19)	1.72 (1.14-2.58)	1.72 (1.11-2.66)	2.40 (1.63-3.53)	2.42 (1.60-3.67)
p-value	**< 0.01**	**0.001**	**0.011**	**0.020**	**< 0.01**	**< 0.01**
Fish						
Non-users	1	1	1	1	1	1
Q 1: 0.33 – 5.92	0.56 (0.39-0.80)	0.57 (0.39-0.83)	0.74 (0.49-1.11)	0.80 (0.52-1.23)	0.56 (0.38-0.84)	0.57 (0.38-0.87)
Q 2: 5.92 – 8.67	0.58 (0.41-0.83)	0.59 (0.41-0.87)	0.52 (0.33-0.81)	0.59 (0.37-0.94)	0.57 (0.39-0.85)	0.53 (0.34-0.81)
Q 3: 8.67 – 14.80	0.64 (0.45-0.90)	0.60 (0.41-0.87)	0.66 (0.43-1.00)	0.61 (0.38-0.96)	0.68 (0.47-1.00)	0.62 (0.41-0.93)
Q 4: 14.80 – 77.40	0.57 (0.40-0.82)	0.54 (0.37-0.79)	0.75 (0.50-1.13)	0.77 (0.50-1.18)	0.44 (0.29-0.68)	0.39 (0.24-0.62)
p-value	**< 0.01**	**< 0.01**	**0.012**	**0.049**	**< 0.01**	**< 0.01**
Cow's milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.17 – 434.81	1.33 (0.57-3.08)	1.24 (0.50-3.09)	2.13 (0.63-7.20)	1.85 (0.53-6.43)	0.97 (0.40-2.35)	0.87 (0.33-2.27)
Q 2: 434.87 – 610.64	1.51 (0.65-3.51)	1.44 (0.56-3.69)	3.02 (0.89-10.19)	2.65 (0.74-9.46)	1.10 (0.45-2.65)	1.00 (0.37-2.71)
Q 3: 610.85 – 743.17	1.74 (0.75-4.03)	1.69 (0.66-4.34)	2.37 (0.70-8.03)	2.09 (0.58-7.52)	1.35 (0.56-3.26)	1.22 (0.45-3.30)
Q 4: 743.33 – 1552.36	1.40 (0.60-3.25)	1.24 (0.48-3.21)	2.18 (0.64-7.39)	1.70 (0.47-6.17)	1.07 (0.44-2.57)	0.91 (0.33-2.47)
p-value	0.278	0.222	0.086	0.079	0.269	0.299
Vegetables						
Non-users	1	1	1	1	1	1
Q 1: 0.02 – 12.75	0.71 (0.36-1.40)	0.69 (0.34-1.40)	0.52 (0.25-1.07)	0.53 (0.25-1.10)	0.50 (0.25-1.00)	0.48 (0.23-0.98)
Q 2: 12.81 – 24.86	0.56 (0.28-1.10)	0.56 (0.27-1.13)	0.44 (0.21-0.90)	0.44 (0.21-0.92)	0.45 (0.22-0.90)	0.43 (0.21-0.88)
Q 3: 24.87 – 43.33	0.82 (0.42-1.63)	0.82 (0.41-1.66)	0.62 (0.30-1.27)	0.62 (0.30-1.30)	0.61 (0.31-1.22)	0.62 (0.30-1.26)
Q 4: 43.50 – 699.32	0.58 (0.30-1.16)	0.58 (0.28-1.17)	0.47 (0.23-0.97)	0.47 (0.23-0.99)	0.50 (0.25-1.00)	0.48 (0.23-0.98)
p-value	**0.024**	**0.04**	0.071	0.095	0.085	0.051
Fish, shellfish and fish products						
Non-users	1	1	1	1	1	1
Q 1: 0.33 – 5.91	0.61 (0.43-0.85)	0.62 (0.43-0.90)	0.75 (0.50-1.12)	0.81 (0.53-1.24)	0.61 (0.42-0.89)	0.63 (0.42-0.94)
Q 2: 5.92 – 8.67	0.64 (0.46-0.90)	0.66 (0.46-0.95)	0.58 (0.38-0.88)	0.64 (0.41-1.01)	0.60 (0.41-0.88)	0.57 (0.37-0.86)
Q 3: 8.67 – 14.83	0.61 (0.43-0.86)	0.57 (0.40-0.83)	0.64 (0.42-0.97)	0.59 (0.37-0.92)	0.64 (0.43-0.93)	0.58 (0.38-0.87)
Q 4: 14.90 – 77.40	0.59 (0.41-0.83)	0.54 (0.37-0.79)	0.73 (0.49-1.09)	0.72 (0.47-1.10)	0.47 (0.31-0.71)	0.43 (0.28-0.68)
p-value	**< 0.01**	**< 0.01**	**0.020**	**0.048**	**< 0.01**	**< 0.01**

(continues)

Table 9, continues

Food variable	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
g/day	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Fruit and berries						
Non-users	1	1	1	1	1	1
Q 1: 0.67 – 43.49	0.45 (0.16-1.27)	0.40 (0.12-1.35)	0.37 (0.13-1.04)	0.38 (0.12-1.21)	0.50 (0.18-1.42)	0.53 (0.17-1.70)
Q 2: 43.50 – 68.80	0.44 (0.15-1.26)	0.38 (0.11-1.29)	0.34 (0.12-0.96)	0.33 (0.10-1.06)	0.46 (0.16-1.29)	0.45 (0.14-1.46)
Q 3: 68.88 – 103.52	0.35 (0.12-0.99)	0.31 (0.09-1.07)	0.29 (0.10-0.83)	0.33 (0.10-1.06)	0.38 (0.13-1.06)	0.37 (0.12-1.21)
Q 4: 103.57 – 471.54	0.35 (0.12-1.00)	0.30 (0.09-1.03)	0.32 (0.11-0.89)	0.33 (0.10-1.06)	0.36 (0.13-1.01)	0.37 (0.11-1.18)
p-value	0.063	0.100	0.153	0.373	0.050	0.067
Potatoes and roots						
Non-users	1	1	1	1	1	1
Q 1: 0.80 – 56.85	0.44 (0.20-0.94)	0.36 (0.15-0.86)	0.30 (0.14-0.65)	0.25 (0.11-0.59)	0.35 (0.16-0.76)	0.30 (0.13-0.71)
Q 2: 56.87 – 87.91	0.47 (0.22-1.02)	0.43 (0.18-1.03)	0.28 (0.13-0.62)	0.26 (0.11-0.62)	0.40 (0.18-0.86)	0.38 (0.16-0.88)
Q 3: 87.92 – 120.17	0.44 (0.20-0.95)	0.37 (0.16-0.88)	0.28 (0.13-0.60)	0.23 (0.10-0.54)	0.36 (0.17-0.77)	0.32 (0.14-0.76)
Q 4: 120.17 – 372.33	0.44 (0.20-0.95)	0.33 (0.14-0.80)	0.31 (0.14-0.67)	0.24 (0.10-0.57)	0.35 (0.16-0.75)	0.28 (0.12-0.66)
p-value	0.307	0.085	**0.027**	**0.020**	0.094	**0.031**
Meat products						
Non-users	1	1	1	1	1	1
Q 1: 0.71 – 25.96	0.76 (0.29-1.95)	0.77 (0.27-2.19)	0.82 (0.28-2.35)	0.64 (0.21-1.95)	0.71 (0.26-1.94)	0.81 (0.27-2.45)
Q 2: 26.01 – 39.98	0.78 (0.30-2.02)	0.78 (0.28-2.22)	0.68 (0.24-1.96)	0.51 (0.17-1.55)	0.85 (0.31-2.30)	0.93 (0.31-2.83)
Q 3: 40.12 – 57.16	0.71 (0.28-1.85)	0.75 (0.26-2.11)	0.78 (0.27-2.25)	0.63 (0.21-1.93)	0.72 (0.26-1.95)	0.83 (0.27-2.51)
Q 4: 57.16 – 340.33	0.70 (0.27-1.81)	0.67 (0.24-1.90)	0.70 (0.24-2.02)	0.50 (0.16-1.52)	0.70 (0.26-1.90)	0.76 (0.25-2.30)
p-value	0.879	0.804	0.741	0.335	0.651	0.774
Dietary fats						
Non-users	1	1	1	1	1	1
Q 1: 0.01 – 3.86	0.84 (0.44-1.60)	0.97 (0.49-1.94)	0.87 (0.42-1.79)	1.06 (0.48-2.35)	0.72 (0.37-1.42)	0.89 (0.43-1.86)
Q 2: 3.87 – 6.30	0.91 (0.48-1.73)	1.07 (0.53-2.14)	0.92 (0.45-1.89)	1.10 (0.49-2.45)	0.72 (0.37-1.41)	0.92 (0.44-1.91)
Q 3: 6.30 – 10.21	0.95 (0.50-1.80)	1.10 (0.55-2.21)	0.73 (0.35-1.51)	0.91 (0.41-2.03)	0.83 (0.42-1.62)	1.01 (0.48-2.11)
Q 4: 10.24 – 75.00	0.94 (0.50-1.79)	0.95 (0.47-1.90)	0.88 (0.43-1.80)	0.92 (0.41-2.07)	0.79 (0.41-1.55)	0.88 (0.42-1.84)
p-value	0.910	0.848	0.689	0.782	0.748	0.920
Beverages and liquid milk products						
Q 1: 33.89 – 883.36	1	1	1	1	1	1
Q 2: 884.38 – 1060.63	1.05 (0.80-1.39)	1.06 (0.77-1.45)	1.03 (0.75-1.41)	0.96 (0.67-1.37)	1.06 (0.78-1.44)	1.11 (0.78-1.57)
Q 3: 1060.71 – 1238.22	1.18 (0.89-1.55)	1.22 (0.88-1.69)	0.89 (0.64-1.22)	0.83 (0.57-1.21)	1.34 (0.99-1.81)	1.44 (1.01-2.05)
Q 4: 1238.24 – 2114.23	1.02 (0.77-1.34)	1.00 (0.72-1.39)	1.02 (0.75-1.40)	0.91(0.62-1.32)	1.17 (0.86-1.58)	1.18 (0.82-1.69)
p-value	0.654	0.512	0.781	0.777	0.235	0.190

[1] IgE ≥0.35 kU/l
[2] Adjusted for energy intake.
[3] Adjusted for energy intake, sex, maternal and paternal vocational education, statistical grouping of home municipality, maternal smoking, mode of delivery, pet in house during first year of life, birth weight, duration of total breastfeeding, number of siblings and parental asthma or allergic rhinitis.

Table 10. Associations between food consumption at 2 years of age and atopic sensitization at 5 years of age.

Food variable g/day	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Egg						
Non-users	1	1	1	1	1	1
Q 1: 0.01 – 2.11	0.69 (0.49-0.96)	0.70 (0.49-0.99)	0.74 (0.51-1.08)	0.78 (0.53-1.16)	0.61 (0.43-0.87)	0.59 (0.41-0.86)
Q 2: 2.12 – 5.17	0.68 (0.49-0.95)	0.70 (0.49-1.00)	0.68 (0.46-0.98)	0.70 (0.47-1.04)	0.59 (0.41-0.84)	0.55 (0.38-0.81)
Q 3: 5.18 – 10.63	0.69 (0.50-0.97)	0.72 (0.50-1.03)	0.74 (0.51-1.07)	0.80 (0.54-1.19)	0.54 (0.38-0.77)	0.52 (0.36-0.77)
Q 4: 10.64 – 90.07	0.59 (0.42-0.83)	0.58 (0.40-0.83)	0.55 (0.37-0.81)	0.52 (0.34-0.79)	0.46 (0.32-0.66)	0.43 (0.29-0.63)
p-value	**0.040**	0.061	0.050	**0.042**	**0.001**	**< 0.01**
Fruit and berry juices						
Non-users	1	1	1	1	1	1
Q 1: 0.01 – 7.20	0.85 (0.63-1.16)	0.73 (0.52-1.02)	0.81 (0.57-1.16)	0.76 (0.52-1.12)	0.84 (0.60-1.18)	0.74 (0.52-1.07)
Q 2: 7.32 – 37.50	1.21 (0.90-1.63)	1.16 (0.84-1.60)	0.87 (0.61-1.24)	0.83 (0.57-1.21)	1.16 (0.85-1.60)	1.08 (0.77-1.52)
Q 3: 37.63 – 87.94	0.83 (0.61-1.12)	0.74 (0.53-1.03)	0.88 (0.62-1.25)	0.79 (0.54-1.16)	0.74 (0.52-1.04)	0.63 (0.44-0.92)
Q 4: 88.60 – 574.92	0.76 (0.56-1.04)	0.68 (0.49-0.95)	0.84 (0.59-1.19)	0.76 (0.52-1.11)	0.65 (0.46-0.93)	0.59 (0.41-0.87)
p-value	0.088	**0.016**	0.721	0.427	**0.027**	**0.007**
Oat and barley						
Non-users	1	1	1	1	1	1
Q 1: 0.02 – 5.10	0.68 (0.49-0.95)	0.65 (0.46-0.94)	0.78 (0.54-1.14)	0.77 (0.51-1.16)	0.61 (0.43-0.88)	0.59 (0.40-0.87)
Q 2: 5.10 – 12.47	0.54 (0.38-0.76)	0.54 (0.38-0.78)	0.54 (0.36-0.80)	0.57 (0.37-0.87)	0.53 (0.37-0.77)	0.49 (0.33-0.74)
Q 3: 12.48 – 22.94	0.90 (0.64-1.25)	0.87 (0.61-1.25)	0.76 (0.52-1.11)	0.79 (0.52-1.20)	0.95 (0.67-1.34)	0.93 (0.64-1.36)
Q 4: 22.95 – 973.33	0.76 (0.54-1.06)	0.77 (0.54-1.10)	0.98 (0.68-1.42)	1.06 (0.71-1.58)	0.60 (0.42-0.86)	0.58 (0.39-0.86)
p-value	**0.003**	**0.007**	**0.011**	**0.021**	**< 0.01**	**< 0.01**
Rye						
Non-users	1	1	1	1	1	1
Q 1: 0.00 – 3.61	0.77 (0.55-1.08)	0.90 (0.63-1.29)	0.68 (0.46-1.01)	0.81 (0.53-1.23)	0.80 (0.56-1.15)	0.87 (0.59-1.28)
Q 2: 3.62 – 7.51	0.74 (0.53-1.03)	0.80 (0.56-1.15)	0.86 (0.59-1.25)	0.96 (0.64-1.44)	0.84 (0.59-1.21)	0.86 (0.59-1.26)
Q 3: 7.52 – 13.05	0.80 (0.57-1.11)	0.78 (0.55-1.12)	0.88 (0.60-1.29)	0.94 (0.63-1.41)	0.69 (0.48-1.00)	0.64 (0.43-0.95)
Q 4: 13.08 – 78.90	0.74 (0.53-1.03)	0.71 (0.49-1.01)	0.77 (0.53-1.13)	0.79 (0.52-1.19)	0.76 (0.53-1.09)	0.67 (0.45-0.99)
p-value	0.396	0.365	0.364	0.691	0.364	0.107
Wheat						
Non-users	1	1	1	1	1	1
Q 1: 0.15 – 15.30	0.52 (0.28-0.97)	0.60 (0.31-1.16)	0.50 (0.26-0.94)	0.58 (0.29-1.13)	0.63 (0.33-1.18)	0.66 (0.34-1.28)
Q 2: 15.30 – 25.03	0.38 (0.20-0.71)	0.44 (0.23-0.85)	0.32 (0.17-0.62)	0.38 (0.19-0.74)	0.56 (0.29-1.05)	0.56 (0.29-1.08)
Q 3: 25.04 – 35.60	0.39 (0.21-0.73)	0.45 (0.23-0.87)	0.35 (0.19-0.67)	0.43 (0.22-0.85)	0.48 (0.26-0.92)	0.48 (0.25-0.93)
Q 4: 35.67 – 107.54	0.39 (0.21-0.73)	0.44 (0.23-0.84)	0.37 (0.20-0.71)	0.45 (0.23-0.88)	0.46 (0.24-0.87)	0.43 (0.22-0.84)
p-value	**0.007**	**0.023**	**0.002**	**0.020**	0.069	**0.027**

(continues)

Table 10, continues

Food variable g/day	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Other cereals						
Non-users	1	1	1	1	1	1
Q 1: 0.02 – 0.92	0.74 (0.51-1.06)	0.69 (0.47-1.01)	0.59 (0.37-0.92)	0.51 (0.32-0.84)	0.90 (0.61-1.33)	0.89 (0.59-1.35)
Q 2: 0.93 – 2.67	0.88 (0.62-1.25)	0.91 (0.62-1.32)	0.95 (0.64-1.42)	0.89 (0.58-1.37)	0.87 (0.59-1.28)	0.93 (0.62-1.42)
Q 3: 2.77 – 7.98	1.04 (0.74-1.47)	1.09 (0.76-1.58)	0.77 (0.50-1.17)	0.69 (0.44-1.08)	1.14 (0.79-1.65)	1.25 (0.84-1.85)
Q 4: 8.00 – 76.17	1.62 (1.15-2.27)	1.59 (1.10-2.29)	1.24 (0.85-1.81)	1.20 (0.80-1.80)	1.55 (1.09-2.22)	1.58 (1.07-2.32)
p-value	**0.013**	**0.019**	0.069	**0.029**	0.097	0.119
Fish						
Non-users	1	1	1	1	1	1
Q 1: 0.55 – 8.02	0.65 (0.45-0.93)	0.66 (0.45-0.96)	0.68 (0.45-1.05)	0.70 (0.45-1.10)	0.62 (0.42-0.93)	0.63 (0.41-0.97)
Q 2: 8.14 – 13.02	0.64 (0.45-0.92)	0.59 (0.40-0.87)	0.67 (0.44-1.03)	0.64 (0.40-1.02)	0.67 (0.45-0.99)	0.59 (0.38-0.90)
Q 3 :13.04 – 20.58	0.79 (0.55-1.11)	0.79 (0.55-1.15)	0.82 (0.55-1.24)	0.95 (0.62-1.46)	0.72 (0.49-1.06)	0.69 (0.45-1.05)
Q 4: 20.70 – 108.53	1.04 (0.74-1.46)	1.03 (0.72-1.47)	1.18 (0.81-1.72)	1.17 (0.78-1.75)	0.79 (0.54-1.15)	0.72 (0.47-1.08)
p-value	**0.020**	**0.022**	0.094	0.152	**0.036**	**0.017**
Fish products						
Non users	1	1	1	1	1	1
Users	0.73 (0.52-1.03)	0.76 (0.53-1.09)	0.72 (0.48-1.08)	0.69 (0.45-1.07)	0.83 (0.58-1.20)	0.84 (0.57-1.25)
p-value	0.069	0.142	0.112	0.094	0.327	0.395
Cow's milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.92 – 419.44	0.75 (0.30-1.92)	0.99 (0.35-2.82)	0.59 (0.22-1.59)	0.60 (0.20-1.81)	0.62 (0.24-1.62)	0.89 (0.30-2.68)
Q 2: 420.35 – 568.52	0.81 (0.32-2.07)	1.04 (0.37-2.98)	0.74 (0.27-2.00)	0.71 (0.24-2.14)	0.58 (0.22-1.51)	0.79 (0.26-2.37)
Q 3: 568.62 – 728.72	0.77 (0.30-1.97)	0.98 (0.34-2.813)	0.56 (0.20-1.51)	0.56 (0.18-1.69)	0.59 (0.23-1.55)	0.77 (0.26-2.33)
Q 4: 729.55 – 1666.03	0.86 (0.34-2.19)	1.10 (0.38-3.16)	0.62 (0.23-1.68)	0.63 (0.21-1.91)	0.65 (0.25-1.70)	0.88 (0.29-2.67)
p-value	0.873	0.954	0.360	0.607	0.781	0.865
Vegetables						
Non-users	1	1	1	1	1	1
Q 1: 0.06 – 18.14	3.05 (0.66-14.14)	2.78 (0.58-13.33)	3.45 (0.44-27.05)	2.71 (0.34-21.69)	3.78 (0.48-29.65)	3.58 (0.44-28.76)
Q 2: 18.15 – 32.31	3.13 (0.68-14.48)	2.67 (0.56-12.78)	3.71 (0.47-29.10)	2.78 (0.35-22.23)	4.15 (0.53-32.58)	3.64 (0.45-29.31)
Q 3: 32.31 – 57.08	2.86 (0.62-13.24)	2.52 (0.53-12.09)	2.81 (0.36-22.12)	2.20 (0.27-17.63)	4.33 (0.55-33.97)	3.83 (0.48-30.82)
Q 4: 57.30 – 924.75	3.09 (0.67-14.32)	2.76 (0.58-13.21)	3.26 (0.42-25.60)	2.48 (0.31-19.83)	4.13 (0.53-32.37)	3.68 (0.46-29.60)
p-value	0.646	0.727	0.384	0.586	0.628	0.793
Fish, shellfish and fish products						
Non-users	1	1	1	1	1	1
Q 1: 0.17 – 7.36	0.65 (0.47-0.91)	0.65 (0.45-0.93)	0.65 (0.43-0.97)	0.65 (0.42-1.00)	0.76 (0.53-1.08)	0.74 (0.51-1.09)
Q 2: 7.53 – 12.97	0.56 (0.40-0.79)	0.51 (0.35-0.74)	0.67 (0.45-0.99)	0.63 (0.41-0.97)	0.58 (0.39-0.85)	0.50 (0.33-0.75)
Q 3: 13.02 – 21.79	0.75 (0.54-1.05)	0.72 (0.51-1.03)	0.76 (0.52-1.12)	0.81 (0.54-1.21)	0.76 (0.53-1.09)	0.69 (0.47-1.02)
Q 4: 21.98 – 108.53	0.96 (0.70-1.32)	0.98 (0.70-1.39)	1.02 (0.71-1.46)	1.02 (0.69-1.50)	0.77 (0.54-1.11)	0.72 (0.49-1.06)
p-value	**0.003**	**0.001**	0.065	0.087	**0.032**	**0.006**

(continues)

Table 10, continues

Food variable g/day	Sensitization to any allergen[1]		Sensitization to any food allergen[1]		Sensitization to any inhalant allergen[1]	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Fruit and berries						
Non-users	1	1	1	1	1	1
Q 1: 0.05 – 55.87	0.67 (0.28-1.62)	0.63 (0.25-1.58)	0.45 (0.18-1.13)	0.44 (0.17-1.14)	0.66 (0.27-1.64)	0.63 (0.25-1.61)
Q 2: 56.16 – 100.39	0.78 (0.33-1.89)	0.68 (0.27-1.71)	0.59 (0.24-1.46)	0.54 (0.21-1.41)	0.64 (0.26-1.58)	0.55 (0.21-1.41)
Q 3: 100.41 – 157.54	0.59 (0.24-1.42)	0.51 (0.20-1.29)	0.43 (0.17-1.07)	0.40 (0.16-1.05)	0.54 (0.22-1.34)	0.45 (0.17-1.16)
Q 4: 157.97 – 862.83	0.51 (0.21-1.24)	0.42 (0.17-1.07)	0.39 (0.16-0.98)	0.35 (0.13-0.91)	0.47 (0.19-1.18)	0.39 (0.15-1.00)
p-value	**0.034**	**0.015**	**0.047**	0.050	0.138	**0.023**
Potatoes and roots						
Non-users	1	1	1	1	1	1
Q 1: 0.13 – 45.93	1.13 (0.46-2.76)	0.97 (0.39-2.45)	0.69 (0.27-1.74)	0.58 (0.22-1.51)	0.81 (0.32-2.05)	0.71 (0.27-1.85)
Q 2: 45.97 – 73.83	1.12 (0.46-2.73)	0.89 (0.35-2.25)	0.57 (0.23-1.45)	0.47 (0.18-1.22)	0.96 (0.38-2.41)	0.77 (0.29-1.99)
Q 3: 73.97 – 108.63	0.90 (0.37-2.19)	0.70 (0.28-1.76)	0.54 (0.21-1.37)	0.41 (0.16-1.08)	0.67 (0.27-1.70)	0.53 (0.20-1.40)
Q 4: 108.74 – 377.78	0.99 (0.41-2.42)	0.80 (0.32-2.01)	0.69 (0.27-1.74)	0.57 (0.22-1.49)	0.67 (0.27-1.70)	0.55 (0.21-1.43)
p-value	0.502	0.264	0.373	0.144	0.112	0.101
Meat products						
Non-users	1	1	1	1	1	1
Q 1: 1.79 – 43.33	3.10 (0.68-14.22)	2.73 (0.58-12.88)	1.70 (0.37-7.81)	1.31 (0.28-6.22)	1.86 (0.41-8.55)	1.77 (0.37-8.37)
Q 2: 43.36 – 60.62	3.32 (0.73-15.20)	2.91 (0.62-13.76)	1.56 (0.34-7.17)	1.26 (0.27-5.97)	2.10 (0.46-9.63)	1.97 (0.42-9.36)
Q 3: 60.70 – 83.69	3.32 (0.72-15.19)	2.93 (0.62-13.83)	1.58 (0.34-7.26)	1.19 (0.25-5.63)	2.03 (0.44-9.33)	1.97 (0.42-9.35)
Q 4: 83.69 – 294.42	3.44 (0.75-15.76)	3.06 (0.65-14.48)	1.67 (0.36-7.65)	1.29 (0.27-6.13)	2.08 (0.45-9.53)	2.03 (0.43-9.63)
p-value	0.572	0.665	0.944	0.977	0.822	0.834
Dietary fats						
Q 1: 0.20 – 8.62	1	1	1	1	1	1
Q 2: 8.63 – 12.52	0.92 (0.69-1.22)	0.84 (0.62-1.15)	0.86 (0.62-1.20)	0.81 (0.57-1.15)	0.91 (0.67-1.24)	0.86 (0.62-1.20)
Q 3: 12.54 – 17.15	0.97 (0.73-1.29)	0.90 (0.66-1.22)	0.91 (0.65-1.26)	0.89 (0.63-1.26)	0.94 (0.69-1.28)	0.84 (0.60-1.17)
Q 4: 17.21 – 85.74	1.06 (0.80-1.41)	0.92 (0.68-1.25)	1.16 (0.84-1.59)	1.06 (0.75-1.50)	1.10 (0.81-1.50)	0.97 (0.70-1.35)
p-value	0.793	0.749	0.306	0.431	0.628	0.657
Beverages and liquid milk products						
Q 1: 274.65 – 894.13	1	1	1	1	1	1
Q 2: 894.18 – 1066.75	1.19 (0.90-1.59)	1.16 (0.86-1.57)	1.07 (0.77-1.48)	1.08 (0.77-1.53)	1.29 (0.95-1.76)	1.25 (0.90-1.74)
Q 3: 1067.10 – 1285.03	1.01 (0.76-1.34)	0.88 (0.65-1.20)	1.10 (0.80-1.53)	0.99 (0.70-1.42)	1.21 (0.82-1.54)	0.99 (0.71-1.39)
Q 4: 1286.44 – 2811.92	1.16 (0.87-1.54)	1.12 (0.83-1.53)	1.03 (0.74-1.43)	1.07 (0.75-1.52)	1.14 (0.83-1.56)	1.06 (0.76-1.49)
p-value	0.498	0.279	0.943	0.945	0.460	0.460

[1] IgE ≥0.35 kU/l

[2] Adjusted for energy intake.

[3] Adjusted for energy intake, sex, maternal and paternal vocational education, statistical grouping of home municipality, maternal smoking, mode of delivery, pet in house during first year of life, birth weight, duration of total breastfeeding, number of siblings and parental asthma or allergic rhinitis.

Table 11. Associations between food consumption at 3 years of age and atopic sensitization at the age of 5 years.

Food variable g/day	Sensitization to any allergen[1] Unadjusted[2]	Sensitization to any allergen[1] Adjusted[3]	Sensitization to any food allergen[1] Unadjusted[2]	Sensitization to any food allergen[1] Adjusted[3]	Sensitization to any inhalant allergen[1] Unadjusted[2]	Sensitization to any inhalant allergen[1] Adjusted[3]
Egg						
Non-users	1	1	1	1	1	1
Q 1: 0.01-2.82	0.74 (0.52-1.04)	0.73 (0.50-1.06)	0.80 (0.55-1.18)	0.81 (0.53-1.22)	0.71 (0.49-1.03)	0.70 (0.47-1.05)
Q 2: 2.84-6.37	0.67 (0.47-0.95)	0.66 (0.46-0.96)	0.57 (0.38-0.84)	0.54 (0.35-0.82)	0.71 (0.49-1.03)	0.71 (0.48-1.05)
Q 3: 6.43-13.18	0.68 (0.48-0.97)	0.69 (0.48-1.01)	0.77 (0.53-1.13)	0.80 (0.53-1.21)	0.66 (0.45-0.95)	0.64 (0.43-0.96)
Q 4: 13.20-90.48	0.47 (0.33-0.67)	0.46 (0.32-0.68)	0.44 (0.29-0.66)	0.45 (0.29-0.70)	0.52 (0.35-0.76)	0.49 (0.33-0.74)
p-value	**0.001**	**0.002**	**< 0.01**	**0.001**	**0.020**	**0.017**
Fruit and berry juices						
Non-users	1	1	1	1	1	1
Q 1: 0.01-15.20	1.19 (0.88-1.61)	1.19 (0.86-1.64)	1.12 (0.79-1.57)	1.13 (0.79-1.64)	1.16 (0.83-1.60)	1.11 (0.78-1.57)
Q 2: 16.67-55.73	0.95 (0.70-1.29)	1.03 (0.75-1.43)	0.89 (0.62-1.27)	0.90 (0.62-1.31)	1.02 (0.73-1.41)	1.09 (0.77-1.55)
Q 3: 56.67-116.67	0.94 (0.69-1.27)	0.88 (0.64-1.23)	0.97 (0.69-1.38)	0.84 (0.57-1.23)	0.93 (0.67-1.30)	0.92 (0.64-1.31)
Q 4: 116.73-712.92	1.09 (0.80-1.47)	1.11 (0.80-1.53)	1.14 (0.81-1.61)	1.24 (0.86-1.78)	1.08 (0.78-1.50)	1.07 (0.75-1.52)
p-value	0.668	0.623	0.755	0.402	0.843	0.893
Oat and barley						
Non-users	1	1	1	1	1	1
Q 1: 0.03-3.89	0.79 (0.57-1.09)	0.74 (0.52-1.05)	0.62 (0.43-0.91)	0.56 (0.37-0.84)	0.85 (0.59-1.21)	0.79 (0.53-1.16)
Q 2: 3.90-9.27	0.97 (0.71-1.34)	0.90 (0.64-1.27)	0.76 (0.53-1.10)	0.67 (0.45-0.99)	1.04 (0.73-1.48)	1.01 (0.69-1.47)
Q 3: 9.32-18.42	1.00 (0.73-1.38)	0.97 (0.69-1.36)	0.76 (0.53-1.09)	0.77 (0.52-1.13)	1.08 (0.76-1.52)	1.03 (0.71-1.50)
Q 4: 18.49-870.13	1.09 (0.79-1.50)	1.04 (0.74-1.47)	0.99 (0.70-1.40)	0.97 (0.66-1.42)	1.16 (0.83-1.64)	1.14 (0.79-1.66)
p-value	0.364	0.319	0.059	**0.019**	0.485	0.399
Rye						
Non-users	1	1	1	1	1	1
Q 1: 0.00-4.50	0.59 (0.41-0.83)	0.58 (0.40-0.85)	0.67 (0.46-0.99)	0.68 (0.45-1.02)	0.53 (0.37-0.77)	0.57 (0.39-0.85)
Q 2: 4.51-9.35	0.52 (0.36-0.74)	0.50 (0.34-0.73)	0.55 (0.37-0.81)	0.55 (0.36-0.84)	0.48 (0.33-0.70)	0.48 (0.32-0.71)
Q 3: 9.35-16.18	0.46 (0.32-0.66)	0.47 (0.32-0.68)	0.41 (0.27-0.61)	0.38 (0.25-0.59)	0.52 (0.36-0.76)	0.56 (0.38-0.82)
Q 4: 16.18-104.28	0.52 (0.37-0.74)	0.54 (0.37-0.79)	0.68 (0.47-1.00)	0.74 (0.49-1.11)	0.41 (0.28-0.60)	0.45 (0.30-0.67)
p-value	**< 0.01**	**0.001**	**< 0.01**	**< 0.01**	**< 0.01**	**0.001**
Wheat						
Non-users	1	1	1	1	1	1
Q 1: 0.33-20.80	0.35 (0.16-0.76)	0.35 (0.16-0.80)	0.33 (0.15-0.69)	0.30 (0.14-0.68)	0.26 (0.12-0.56)	0.28 (0.13-0.63)
Q 2: 20.82-31.70	0.39 (0.18-0.85)	0.39 (0.17-0.88)	0.33 (0.16-0.70)	0.32 (0.15-0.71)	0.29 (0.14-0.62)	0.29 (0.13-0.65)
Q 3: 31.72-43.52	0.27 (0.13-0.59)	0.27 (0.12-0.61)	0.22 (0.10-0.47)	0.22 (0.10-0.49)	0.26 (0.12-0.55)	0.26 (0.12-0.57)
Q 4: 43.56-114.28	0.33 (0.15-0.72)	0.30 (0.13-0.67)	0.29 (0.14-0.62)	0.27 (0.12-0.59)	0.28 (0.13-0.60)	0.27 (0.12-0.59)
p-value	**0.007**	**0.007**	**0.001**	**0.004**	**0.012**	**0.022**

(continues)

Food variable g/day	Sensitization to any allergen[1] Unadjusted[2]	Adjusted[3]	Sensitization to any food allergen[1] Unadjusted[2]	Adjusted[3]	Sensitization to any inhalant allergen[1] Unadjusted[2]	Adjusted[3]
Other cereals						
Non-users	1	1	1	1	1	1
Q 1: 0.00-1.00	1.03 (0.74-1.42)	0.98 (0.70-1.39)	1.24 (0.86-1.78)	1.23 (0.83-1.80)	0.84 (0.58-1.22)	0.81 (0.55-1.20)
Q 2: 1.00-3.17	0.75 (0.53-1.06)	0.79 (0.55-1.13)	0.71 (0.47-1.08)	0.73 (0.47-1.13)	0.85 (0.58-1.22)	0.87 (0.58-1.29)
Q 3: 3.20-7.99	1.25 (0.90-1.72)	1.26 (0.90-1.78)	1.27 (0.89-1.83)	1.21 (0.82-1.80)	1.14 (0.80-1.61)	1.17 (0.81-1.70)
Q 4: 8.00-87.37	1.26 (0.91-1.74)	1.42 (1.00-2.01)	1.42 (0.99-2.02)	1.52 (1.04-2.23)	1.20 (0.85-1.70)	1.36 (0.94-1.98)
p-value	0.111	0.079	**0.045**	0.055	0.420	0.199
Fish						
Non-users	1	1	1	1	1	1
Q 1: 0.39-8.92	0.97 (0.69-1.37)	0.87 (0.59-1.28)	0.83 (0.55-1.25)	0.69 (0.43-1.11)	1.17 (0.81-1.68)	1.01 (0.67-1.52)
Q 2: 8.96-14.69	0.82 (0.58-1.18)	0.83 (0.57-1.21)	0.89 (0.59-1.33)	0.85 (0.55-1.31)	0.67 (0.44-1.00)	0.70 (0.46-1.08)
Q 3: 14.70-24.10	0.74 (0.52-1.07)	0.78 (0.53-1.14)	0.83 (0.55-1.26)	0.92 (0.60-1.41)	0.70 (0.47-1.05)	0.70 (0.46-1.07)
Q 4: 24.19-133.80	0.60 (0.42-0.88)	0.57 (0.38-0.85)	0.58 (0.37-0.91)	0.57 (0.35-0.93)	0.59 (0.38-0.89)	0.53 (0.33-0.83)
p-value	0.054	0.067	0.169	0.132	**0.011**	**0.025**
Fish products						
Non users	1	1	1	1	1	1
Users	0.87 (0.64-1.18)	0.91 (0.66-1.25)	1.09 (0.78-1.53)	1.17 (0.82-1.67)	0.79 (0.56-1.11)	0.81 (0.56-1.16)
p-value	0.366	0.55	0.605	0.394	0.175	0.249
Cow's milk products						
Non-users	1	1	1	1	1	1
Q 1: 0.01-420.23	0.28 (0.14-0.58)	0.30 (0.14-0.65)	0.21 (0.11-0.43)	0.24 (0.11-0.52)	0.35 (0.18-0.69)	0.29 (0.14-0.62)
Q 2: 421.11-567.49	0.23 (0.11-0.48)	0.26 (0.12-0.56)	0.16 (0.08-0.32)	0.17 (0.08-0.36)	0.32 (0.16-0.63)	0.27 (0.13-0.58)
Q 3: 567.60-700.71	0.26 (0.13-0.54)	0.29 (0.14-0.64)	0.18 (0.09-0.37)	0.21 (0.10-0.44)	0.32 (0.16-0.63)	0.27 (0.13-0.57)
Q 4: 701.60-1719.00	0.30 (0.15-0.61)	0.34 (0.16-0.74)	0.20 (0.10-0.40)	0.23 (0.11-0.50)	0.35 (0.18-0.69)	0.30 (0.14-0.64)
p-value	**0.002**	**0.010**	**< 0.01**	**< 0.01**	**0.021**	**0.015**
Vegetables						
Q 1: 0.13-19.12	1	1	1	1	1	1
Q 2: 19.28-38.21	0.87 (0.65-1.16)	0.89 (0.66-1.21)	0.77 (0.55-1.07)	0.77 (0.54-1.10)	1.04 (0.76-1.43)	1.05 (0.75-1.46)
Q 3: 38.26-63.30	1.00 (0.74-1.31)	1.05 (0.78-1.43)	0.97 (0.70-1.33)	0.99 (0.70-1.40)	1.13 (0.83-1.53)	1.22 (0.88-1.70)
Q 4: 63.33-587.09	1.04 (0.78-1.38)	1.09 (0.80-1.49)	0.87 (0.63-1.20)	0.90 (0.63-1.28)	1.17 (0.86-1.59)	1.16 (0.82-1.63)
p-value	0.652	0.576	0.399	0.454	0.761	0.634
Fish, shellfish and fish products						
Non-users	1	1	1	1	1	1
Q 1: 0.09-7.95	0.96 (0.70-1.33)	0.88 (0.62-1.25)	0.95 (0.66-1.38)	0.84 (0.56-1.26)	0.94 (0.66-1.33)	0.82 (0.56-1.19)
Q 2: 7.96-14.04	0.84 (0.61-1.16)	0.83 (0.59-1.17)	0.88 (0.60-1.27)	0.82 (0.55-1.23)	0.74 (0.52-1.06)	0.79 (0.54-1.15)
Q 3: 14.04-24.58	0.84 (0.61-1.17)	0.86 (0.61-1.21)	0.95 (0.66-1.38)	0.98 (0.66-1.44)	0.85 (0.60-1.21)	0.82 (0.57-1.20)
Q 4: 24.60-133.80	0.60 (0.42-0.84)	0.59 (0.41-0.85)	0.63 (0.42-0.94)	0.66 (0.43-1.02)	0.54 (0.37-0.80)	0.50 (0.33-0.76)
p-value	0.052	0.076	0.261	0.372	**0.026**	**0.025**

(continues)

Table 11, continues

Food variable g/day	**Sensitization to any allergen[1]**		**Sensitization to any food allergen[1]**		**Sensitization to any inhalant allergen[1]**	
	Unadjusted[2]	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**	**Unadjusted[2]**	**Adjusted[3]**
Fruit and berries						
Non-users	1	1	1	1	1	1
Q 1: 0.15-53.87	1.30 (0.55-3.10)	0.87 (0.34-2.19)	0.97 (0.38-2.51)	0.72 (0.27-1.97)	2.01 (0.67-5.99)	1.38 (0.45-4.30)
Q 2: 53.91-110.86	1.11 (0.47-2.63)	0.81 (0.32-2.06)	0.85 (0.33-2.19)	0.67 (0.25-1.83)	1.59 (0.53-4.77)	1.20 (0.39-3.73)
Q 3: 110.92-180.21	1.16 (0.49-2.77)	0.81 (0.32-2.06)	0.87 (0.34-2.24)	0.64 (0.23-1.74)	1.95 (0.65-5.81)	1.42 (0.46-4.40)
Q 4: 180.29-850.89	1.26 (0.53-2.99)	0.91 (0.36-2.32)	0.93 (0.36-2.39)	0.75 (0.27-2.05)	2.02 (0.68-6.02)	1.46 (0.47-4.54)
p-value	0.785	0.923	0.924	0.818	0.379	0.769
Potatoes and roots						
Non-users	1	1	1	1	1	1
Q 1: 0.26-46.14	1.95 (0.75-5.06)	2.00 (0.70-5.75)	1.74 (0.58-5.23)	1.42 (0.45-4.43)	1.48 (0.54-4.09)	1.57 (0.50-4.91)
Q 2: 46.18-74.27	1.71 (0.66-4.44)	1.88 (0.65-5.40)	1.45 (0.48-4.39)	1.22 (0.39-3.82)	1.29 (0.47-3.55)	1.48 (0.47-4.64)
Q 3: 74.30-180.70	1.74 (0.67-4.52)	1.72 (0.60-4.94)	1.48 (0.49-4.47)	1.14 (0.36-3.58)	1.36 (0.49-3.75)	1.40 (0.45-4.38)
Q 4: 108.70-364.57	1.64 (0.63-4.27)	1.60 (0.56-4.61)	1.29 (0.43-3.91)	1.04 (0.33-3.26)	1.39 (0.50-3.83)	1.42 (0.45-4.44)
p-value	0.568	0.470	0.444	0.504	0.875	0.906
Meat products						
Non-users	1	1	1	1	1	1
Q 1: 0.62-48.34	1.07 (0.31-3.72)	1.35 (0.33-5.52)	1.39 (0.29-6.54)	1.15 (0.23-5.66)	0.66 (0.19-2.28)	0.85 (0.21-3.47)
Q 2: 48.39-67.42	1.03 (0.30-3.60)	1.31 (0.32-5.36)	1.40 (0.30-6.60)	1.13 (0.23-5.58)	0.60 (0.17-2.09)	0.73 (0.18-3.01)
Q 3: 67.46-92.50	0.96 (0.28-3.35)	1.19 (0.29-4.85)	1.26 (0.27-5.96)	0.94 (0.19-4.63)	0.61 (0.18-2.13)	0.78 (0.19-3.22)
Q 4: 92.59-500.22	1.05 (0.30-3.66)	1.35 (0.33-5.53)	1.31 (0.28-6.20)	1.03 (0.21-5.11)	0.70 (0.20-2.43)	0.98 (0.24-4.03)
p-value	0.963	0.900	0.958	0.806	0.789	0.491
Dietary fats						
Q 1: 0.26-11.47	1	1	1	1	1	1
Q 2: 11.48-15.96	0.93 (0.70-1.23)	0.93 (0.69-1.26)	0.98 (0.71-1.35)	1.03 (0.73-1.45)	0.95 (0.69-1.29)	0.92 (0.66-1.28)
Q 3: 15.98-21.68	0.92 (0.70-1.23)	0.92 (0.68-1.25)	0.83 (0.60-1.15)	0.83 (0.58-1.19)	0.91 (0.67-1.24)	0.89 (0.64-1.25)
Q 4: 21.72-94.22	0.90 (0.68-1.20)	0.83 (0.61-1.21)	0.86 (0.62-1.19)	0.84 (0.59-1.19)	1.02 (0.75-1.39)	0.95 (0.68-1.32)
p-value	0.900	0.67	0.601	0.499	0.883	0.919
Beverages and liquid milk products						
Q 1: 167.27-892.38	1	1	1	1	1	1
Q 2: 892.46-1068.55	0.80 (0.61-1.07)	0.76 (0.56-1.03)	0.77 (0.56-1.06)	0.80 (0.56-1.12)	0.88 (0.65-1.20)	0.78 (0.56-1.09)
Q 3: 1068.62-1254.70	1.03 (0.78-1.36)	1.03 (0.77-1.40)	0.89 (0.65-1.23)	0.92 (0.65-1.30)	1.02 (0.75-1.38)	1.00 (0.72-1.38)
Q 4: 1255.69-2376.67	0.84 (0.63-1.12)	0.87 (0.64-1.18)	0.77 (0.55-1.06)	0.83 (0.59-1.18)	0.88 (0.65-1.20)	0.88 (0.64-1.23)
p-value	0.231	0.171	0.300	0.569	0.670	0.427

[1] IgE ≥0.35 kU/l
[2] Adjusted for energy intake.
[3] Adjusted for energy intake, sex, maternal and paternal vocational education, statistical grouping of home municipality, maternal smoking, mode of delivery, pet in house during first year of life, birth weight, duration of total breastfeeding, number of siblings and parental asthma or allergic rhinitis.

6 DISCUSSION

6.1 Summary of the findings

The results from this study show a strong inverse association between consumption of several food items during the first 3 years of life and allergic sensitization at the age of 5 years. Specifically consumption of cereals (oat, barley, wheat and rye) were inversely associated with atopic sensitization to any allergen, any food allergen and any inhalant allergen. Consumption of cow's milk products was as well associated with decreased risk of atopic sensitization to any allergen, any food allergen and any inhalant allergen. Conversely, consumption of other cereals (rice, buckwheat, corn flour and millet), were associated with increased risk of atopic sensitization, and this was the only direct association found in this study.

6.2 Strengths and weaknesses

The strength of this study comes from the large number of study subjects, the duration of the follow-up, the longitudinal collection of dietary data and the quality of the food record data. At the moment, this is the only study on this topic that has assessed dietary data longitudinally in relation to the development of allergy in children. The strength of the nutritional data when assessed using food records is, that the quality and reliability of data increase with the number of days and time points the food records are collected. A further strength of this study is its prospective nature given that the assessment of dietary data was undertaken prior to the assessment of the endpoint. This offered the opportunity to examine the temporal relationship between food consumption and subsequent development of atopic sensitization.

Some of the weaknesses of this study include the confounding factors related to dietary assessments. Despite the method of collecting the data or meticulousness of the recording, none of the methods which directly measure food intake, can give accurate data on the actual dietary intake (Tricon et al. 2006). Nevertheless, since food intake cannot be accurately and precisely measured, the level of accuracy used in recording the dietary data assessed in the current study, can be considered to be adequate.

As for endpoints, only the measurements of IgE antibodies were included in this study. Several other studies have included a large number of clinical symptoms instead of, or along with IgE measurements (Nafstad et al. 2003, Nagel et al. 2010, Loss et al. 2011, Magnusson et al. 2013, Roduit et al 2014). Although, all of those who sensitize to allergens do not develop clinical symptoms of allergy, the measurements of allergen specific IgE antibodies in the blood have been known to be highly predictive of allergy development in the future (Tricon et al. 2006) and therefore should be studied as an endpoint on its own as well as alongside with clinical symptoms.

6.2.1 Subjects and generalizability

The study population composed of almost equally from both genders; 51.6 % boys and 48.4 % girls. Other characteristics seemed to also reflect quite well on the general population and therefore the generalizability of the results is applicable.

The recruitment for this study was based on children having the HLA-DQB1–conferred susceptibility to type 1 DM. This should not create selection bias since knowledge of this susceptibility should not affect lifestyle or other choices within the families. Type 1 diabetes occurs only in a fraction (approx. 2 % in the DIPP–study) of the children who have this susceptibility. The data were collected before the outcomes and therefore the collection of the data did not affect the dietary variables. The children participating in the allergy study were generally similar to those who refused to participate, and therefore should not cause selection bias either.

Despite the fact that the children in this study come from Tampere area, the results can be generalized to Finnish population, since the differences in lifestyle and genetics are small within the country.

6.3 Comparison with previous studies

The findings of this study support previous findings of the consumptions of vegetables, milk and fish and the reduced risk of allergic diseases (Nafstad et al. 2003, Kull et al. 2006, Waser et al. 2007, Loss et al. 2011, Rosenlund et al. 2011). Previous findings although being similar, have been much more restricted in terms of food variables and the length of the follow-up. This study provides strong evidence of food consumption influencing the atopic sensitization, which has not been concluded to this extend in previous studies.

Comparison to other studies is difficult since the studies of the food consumption and atopic sensitization or allergy development have not been conducted widely. The execution of the studies and the characteristics of the study subjects also vary greatly. Many of the few studies conducted in the field of allergies and food consumption have been with cross sectional design (Nafstad et al. 2003, Waser et al. 2006, Nagel et al 2010, Loss et al. 2011, Rosenlund et al.

2011). A prospective cohort design has rarely been used in studies assessing early life food consumption and allergies, the number of studies being almost non-existent at the moment.

Great variety of different dietary assessment methods have also been used, of which parental food frequency questionnaire seems to be the most common (Kull et al. 2006, Waser et al. 2006, Nagel et al. 2010, Loss et al. 2011, Rosenlund et al. 2011, Magnusson et al. 2013). In this study a 3-day food record was used to collect the food consumption data. Food frequency questionnaire is less time consuming and perhaps easier for the parent, but does not give as accurate information as food records from several days, and is usually done only at one time point. Retrospective studies always rely on the memory of the study subjects, or in this case the parents of the children participating and creates a great possibility for an error caused by false memory.

The age of the study subjects in previous studies have varied from newborns to school children up to 12 years of age (Nafstad et al. 2003, Waser et al. 2006, Rosenlund et al. 2011, Magnusson et al. 2013). Only a couple of studies have included newborns with a 3 to 5 years of follow up (Nafstad et al. 2003, Kull et al. 2006, Roduit et al. 2014). According to the evidence, it seems that infancy and early childhood might be the most important period of life in terms of immunological development (Molloy et al. 2013). It also seems that the follow-up should be at least a couple of years since not all children develop atopic sensitization during the first year of life, not to mention clinical outcomes which could take several years or even a decade to develop.

In the present study, most of the background characteristics did not seem to influence sensitization, despite the opposite results in several previous studies (Muche-Borowski et al. 2009, Pfefferle and Renz 2014). Nevertheless, it seems that in this, as for other studies, the influence of the genetics (parental allergic condition) is strong.

6.4 Possible explanations of the findings

At the age of 3 months there was no association found between diet and sensitization. This could be due to the minimal consumption of complementary foods and the high number of non-users in most of the food groups analyzed. Many of the food groups could not be analyzed at all, due to the lack of users of these foods. Complementary foods are generally introduced to infants at 4-6 months of age as recommended in the Finnish national nutrition guidelines for infants and young children (Hasunen et al. 2004) and this common practice was evident also in the data we assessed.

Consumption of other cereals (rice, buckwheat, corn flour and millet) were associated with increased risk of atopic sensitization, being the only positive associations observed in this study. The positive associations were evident only in the highest quartiles, which could be due to other factors than the cereals themselves. The results could be explained by restrictions in the diet concerning traditional Finnish cereals (e.g. wheat) which are replaced for instance with millet and buckwheat. These restrictions could for instance be due to a food allergy. Children in the lowest quartiles are most likely using rice and corn since the amounts used are considerably low (< 8 g/day).

7 CONCLUSIONS AND FUTURE IMPLICATIONS

7.1 Conclusions

In conclusion, the evidence from this study support the suggestion that food consumption during early life may influence the development of allergy in childhood, thus providing the opportunity that dietary modification interventions would be beneficial for the primary prevention of allergy in children. However, the relevance of different foods seems to vary greatly and when some foods seem to have a strong associations, others seem to have no associations at all. The results of this study indicate that the consumption of cereals (oats, barley, rye and wheat) seem to reduce the risk of sensitization to common food and inhalant allergens. In addition, the consumption of fish, egg, potatoes and roots and cow's milk may also reduce the risk of atopic sensitization.

On the contrary, the consumption of other cereals (rice, buckwheat, corn flour and millet) were found to increase the risk of atopic sensitization, being the only food directly associated with the risk of atopic sensitization. The reason for this observation is unclear, but a possible explanation may be that the consumption of 'other cereals' may be associated with the risk of allergy through other pathways related to food choices such as social behavior.

All things considered, in the light of the findings of the present study, which are in line with other previous studies, the current nutritional recommendations of diverse introduction to solid foods seem to be in place while waiting for more data.

7.2 Future implications

For future studies existing food allergy and suspected allergy should be considered as potential confounding factors. Food allergies change the diet of the child and could also show up in IgE-measurements and therefore may confound the result of the analysis and lead to reverse causation. Specifically cow's milk allergy changes the child's diet dramatically and is relatively common food allergy in children. Approximately 2-3 % of under 3-year old Finnish children have cow's milk allergy (Food allergy (children): Current Care Guideline 2012).

The cereals should be looked at separately, due to the strong inverse associations for atopic sensitization in this study. Especially gluten containing cereals and gluten free cereals should be analyzed separately. It would also be beneficial to take into account the nutrients in addition to foods. This way it might be possible to determine which particles in the foods are effective.

To be able to assess how well the measured IgE antibodies predict future allergies, it would be useful to collect data of clinical manifestations of allergic diseases from the study subjects, such as allergic rhinitis, eczema and doctor diagnosed food allergy. This would give additional information of how diet affects these allergic diseases and also how well the IgE measurements reflect the development of clinical symptoms in the future in the current population. High risk children (children with at least one parent with allergic condition) could be analyzed separately to get a better idea of how important factor the genetic susceptibility is in this population.

The population of this study comprised of children from Tampere region. For future studies it would be beneficial to include all the data available to create a larger study population from more diverse region and therefore achieve better generalizability. In addition to the Tampere region the complete study population of DIPP nutrition study comprised of children from Oulu region.

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