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EAACI position paper on diet diversity in pregnancy, infancy and childhood: Novel concepts and implications for studies in allergy and asthma

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Abstract

To fully understand the role of diet diversity on allergy outcomes and to set standards for conducting research in this field, the European Academy of Allergy and Clinical Immunology Task Force on Diet and Immunomodulation has systematically explored the association between diet diversity and allergy outcomes. In addition, a detailed narrative review of information on diet quality and diet patterns as they pertain to allergic outcomes is presented. Overall, we recommend that infants of any risk category for allergic disease should have a diverse diet, given no evidence of harm and

some potential association of benefit in the prevention of particular allergic outcomes. In order to harmonize methods for future data collection and reporting, the task force members propose relevant definitions and important factors for consideration, when measuring diet diversity in the context of allergy. Consensus was achieved on practice points through the Delphi method. It is hoped that the definitions and considerations described herein will also enable better comparison of future studies and improve mechanistic studies and pathway analysis to understand how diet diversity modulates allergic outcomes.

Word count: 5073

Introduction

To increase our understanding of the complex relationship between nutrients and other essential components of food, there has been a growing interest in taking a whole diet approach when studying disease outcomes. In particular, research focusing on diet diversity has received significant attention due to its potential role in the prevention of allergic diseases. Diet diversity is defined as the number of different foods or food groups consumed over a given reference period.[1] Diet variety, a term often used in the literature, is considered synonymous with diet diversity.[1] A list of nutritional definitions relevant to this paper are summarized in box 1.

As nutrients and foods are not eaten in isolation and an intake of one food or nutrient may inadvertently lead to reduced intake of another, dietary diversity is a challenging area of research. The task force appreciates that intake of single food or nutrients may also play an important role in the development of allergic diseases. One such example is the study by Bisgaard et al.[10] showing that supplementation with omega-3 fatty acids in the third trimester of pregnancy reduced the risk of persistent wheeze or asthma. The control group was however taking olive oil, a key component and indicator of the Mediterranean diet, which could be attributable to reduced allergy outcomes even in the control group.[11,12]

The mechanistic basis for how diet diversity potentially affects allergy outcomes needs further clarification[13-15], but may ultimately be mediated through a multitude of immune tolerance mechanisms including T and B regulatory cells, immune regulatory cytokines and suppressed IgE antibodies as demonstrated in other allergen tolerance models.[16] Possible mechanisms by which diet diversity could affect allergy outcomes are summarized below:

1) It is postulated that a more diverse diet may indirectly affect tolerance development via an effect on the microbiome. This is supported by studies showing that increased diet diversity leads to increased microbial diversity in the elderly[17] and in infants during the introduction of solid food.[18] Increased microbial diversity[19] or abundance of certain bacteria[20] has been associated with reduced allergy outcomes. However, there is a paucity of information linking diet diversity, microbial diversity and allergy outcomes.

2) Diet diversity does not provide a finite indication of diet quality, but it may be associated with increased nutrient intake whereas a more diverse diet may indirectly affect allergy outcomes by providing nutrients associated with prevention of allergic diseases such as omega-3 fatty acids and non-digestible fibers.[21,22]

3) A more diverse diet may also lead to exposure of different food antigens that impact development of immune tolerance, though this may be "low dose" exposure,[23] supporting recent randomized controlled trials regarding early allergen introduction.[24,25,26,27]

The focus of this paper is to systematically review and critically address the current knowledge of the association between *diet diversity and allergy outcomes*. To fully understand the role of diet diversity on allergy outcomes and to set standards for conducting research in this field, this review will explore the concept of diet diversity and describe this in the context of other dietary measures, such as diet quality and diet patterns. This is followed by a systematic search and review of the association between diet diversity and allergy outcomes. An overview of information on diet quality and diet patterns as they pertain to allergic outcomes is also given. Finally, this European Academy of Allergy and Clinical Immunology (EAACI) Task Force proposes factors for consideration and relevant definitions when measuring diet diversity in the context of allergy, with the aim to standardize methods for future data collection and reporting. The authors of this taskforce hope that this paper and it's recommendations (table 1) will also better enable comparison of future studies and improve mechanistic studies and pathway analysis.

Methods

The EAACI taskforce was formed in 2017 and met in person in 2017 and 2018 at the EAACI annual Congress to discuss proposed publications on the role of diet diversity and allergic outcomes. A

search of the literature regarding diet quality, diet diversity, and food patterns to inform future practice and research relating to allergic outcomes was performed. The full literature search and terms are listed in online supplementary file 1. Studies on single nutrients or single foods were excluded from the search as the review focused on diet diversity and quality opposed to single nutrient/food outcomes.

Searches 1 and 2 were conducted to give background information on the use of diet diversity and diet quality in characterizing nutrition intake and healthy/nutrition outcomes. Search 1 focused on diet diversity in pregnancy, infancy, childhood and in households compared to health/nutrition outcomes (Section 1). Search 2 focused on diet quality in pregnancy, infancy, childhood, and households compared to health/nutrition outcomes (Section 2). Search 3 and 4 included a systematic literature search regarding diet diversity, diet quality and food patterns compared to allergy outcomes. Search 3 focused on diet diversity and diet patterns during pregnancy and allergy outcomes in the infant (Section 3), whereas search 4 focused on diet diversity and food patterns during infancy and childhood and allergy outcomes (Section 4). Key opinion leaders in the field of diet diversity and diet quality were contacted to enquire about guideline papers or book chapters in this field. A modified Delphi panel was used among the task force members to provide consensus on key themes and potential recommendations.[66]

Section 1: Overview on the use of diet diversity to measure nutrition intake in pregnancy, infancy or childhood

Historically, studies on diet diversity investigation 1) child nutrient intake or 2) growth status, and 3) a number of other health outcomes. Studies from both developed[67] and developing countries[29,68] have noted that an increase in diet diversity was associated with an increase in nutrient adequacy. Studies focusing on diet diversity have shown that an increase in diet diversity was associated with better growth indices in young children using height, weight, skin fold thickness and length for age or height for age z-scores to describe stunting, underweight and overweight [69-76], though this might be confounded by socio-economic status. The association between diet diversity and other health outcomes in pregnancy, infancy and childhood(e.g. obesity) [77-79] has also been studied and is summarized in online supplementary tables S1a-d.

Diet diversity can be measured by counting individual foods[31,34,68,74,79-81], food group [29,31,71-73,75,76,78,82-89] or foods within a group[69,70,90,91], and can be measured over a time period ranging from the previous

24 hours (24-hour recalls) past 24 hours[34,68-72,75,77,81,83] or over a 7-day period [70,76,79,82,88,90-92] to intake over one year. Food intake data collected once[34,69-71,75,77,83] or a number of times [68,72,81] as summarized in online supplementary tables S1a-d. Factors that should be considered when measuring diet diversity are summarized in table 1.

Section 2: Overview on the use of diet quality in measuring nutrition intake

The term diet quality is broadly used as an umbrella term to describe a healthy, balanced, nutritious diet for optimal health characterized by limited amounts of fat, saturated fat, cholesterol, sodium, and refined sugars, and meeting the recommended amounts of fruits, vegetables, and whole grain products.[52] Diet quality is often described using a nutrition index, although food patterns e.g. the Mediterranean diet are also often referred to as indicators of diet quality. The purpose of diet indices is to synthesize a large amount of dietary information into a single useful indicator.[93] Over the years, various indices have been developed to measure diet quality, amended and validated to evaluate healthy dietary patterns such as the healthy eating index (HEI) score[51], the Meditteranean diet score[94], as well as more complex indices[62,95,96]. Scoring is typically based on consumption of nutrients, foods or both[97] though there is wide heterogeneity in methods used. Supplementary Table S2 summarizes the most commonly used dietary indices in pregnancy, infancy and childhood.

Section 3: Diet diversity and diet quality (indices and diet patterns) during pregnancy and allergy outcomes in the infant

Diet diversity and diet quality have been used to find associations between dietary intake and allergy outcomes in either pregnancy or infant's early life or both. We conducted a systematic review of the literature to identify relevant studies, investigate the measures used and describe any associations found with allergy outcomes.

Diet diversity in pregnancy and allergy outcomes

While this is an important relationship to understand, no studies have been identified exploring an association between diet diversity in pregnancy and allergy outcomes.

Diet quality in pregnancy and allergy outcomes

Studies on diet quality in pregnancy and allergic diseases have used the Mediterranean diet score [98-102] or a modified version of the HEI in pregnancy[103,104] to investigate an association with allergic outcomes.

Mediterranean diet in pregnancy and allergy outcomes

Four papers from longitudinal birth cohort studies[98-100,103] (two from Spain, one from Greece, one from the USA) studied the association between Mediterranean diet patterns and atopic outcomes in the offspring (online supplementary table S3)**.** Typically, a diet score is developed and dietary information, obtained from food recalls (food diaries, 24 hr recalls, food diaries) are used to calculate the Mediterranean diet score**.**[94] In two studies, dairy intake[99,100] was added to the Mediterranean diet score. All studies adjusted their analyses for common confounders, though these varied between studies. Two studies included the use of vitamin/mineral supplements in their dietary analysis[98,103]; in one study it was unclear if the use of supplements was included in the analyses[99] and one study adjusted for mineral/vitamin intake only in the statistical analyses.[100]

Outcomes reported in the infants were wheeze in all studies[98-100,103], asthma in one study [103], and rhinitis, atopic dermatitis and/or eczema in three studies[98-100] Sensitisation to food/aero-allergens was determined in two studies.[100,103] None of these studies reported on food allergy as an outcome, highlighting a true deficiency in the literature. All outcome measures were parental reported and/or doctors diagnosed.

In 3 of the 4 studies[98,99,103], a Mediterranean diet pattern during pregnancy was not associated with the development of atopic diseases in the offspring. However, one study[100] indicated that the Mediterranean diet was associated with reduced prevalence of persistent wheeze, atopic wheeze and atopy.

Other dietary patterns or indices used in pregnancy

Investigating dietary patterns other than the Mediterranean diet, we found four longitudinal birth cohort studies;[104-107] three studies using semi-quantitative FFQs, from which the diet patterns were analysed and one used a 24-hour recall[105] (supplementary table S4). In three studies, the use of vitamin/mineral supplements was not reported and in one the use of supplements was excluded.[104-

[107] All studies adjusted their analyses for common confounders, although confounders varied widely between studies.

In one study, the Alternate Healthy Eating Index modified for pregnancy (AHEI-P) developed by Rifas et al.[108] was used to examine associations with allergic outcomes[104] and in three studies food patterns were studied.[105-107] In these three studies, principal components analysis was used to assess individual food intake and the following food patterns emerged as associated with allergic outcomes:

- Seafood and Noodle pattern (noodle soup, noodles with sauce, fish, seafood and seafood products);
- Vegetable, Fruit and white Rice pattern (vegetables, fruit, whole grain bread and white rice with minimal processed foods/meats);
- Pasta, Cheese and Processed meat pattern (pasta, processed grains, cheese and processed meats in pregnancy)[105];
- Healthy pattern (high consumption of green and yellow vegetables, seaweed, mushrooms, white vegetables, pulses, potatoes, fish, sea products, fruit, and shellfish and low intake of confectioneries and soft drinks);
- Western pattern (high consumption of vegetable oil, salt-containing seasonings, beef and pork, processed meat, eggs, chicken, and white vegetables and low intake of fruit, soft drinks, and confectioneries);
- Japanese pattern (high consumption of rice, miso soup, sea products, and fish and low intake of bread, confectioneries, and dairy products)[106];
- Health conscious pattern (salad, fruit, fruit juices, rice, pasta, oat/bran, fish);
- Traditional pattern (vegetables, red meat and poultry);
- Processed pattern (meat pies, sausages, burgers, fried food);
- Vegetarian pattern (meat substitutes, pulses, nuts, herbal tea);
- Confectionary (chocolate, sweets, biscuits, cakes and puddings).[107]

Outcomes measured were asthma[105,107], eczema[105,106], rhinitis[105] and sensitisation to food/aero-allergens[48,104,105]. The only positive associations reported were reduced sensitization due to the seafood and noodle pattern[105] and reduced wheeze due to the western diet pattern.[106]. The Seafood and Noodle pattern[105] was associated with a reduced risk of developing allergen sensitization at

both 18 months [odds ratio (95% confidence interval): 0.7 (0.5-0.9)] and 36 months [odds ratio (95% confidence interval) 0.7 (0.6 -0.9)][105]; The maternal Western diet pattern was associated with a reduced risk of wheeze, and in adjusted analysis the OR between extreme quartiles was 0.59 (95% CI: 0.35–0.98, p for trend = 0.02)[106,107] Once again, no study looked at food allergy as an outcome.

Section 4: Diet Diversity during infancy and allergy outcomes in the infant

Diet diversity and allergen sensitization

IgE sensitization is a commonly used (but limited and imprecise) marker of clinical allergy. Roduit et al.[16] investigated the association between diet diversity and allergic disease and collected sensitization data based on specific IgE (table 2) in the Protection Against Allergy Study in Rural Environments (PASTURE) prospective cohort study, which enrolled children from Austria, Finland, France, Germany and Switzerland. Diet diversity in this study was defined as the 15 foods commonly eaten by 80% of the children in the study in the first year of life: any cow's milk, yogurt, other milk product; eggs; nuts; vegetables or fruits; cereals; bread; meat; fish; soy; margarine or butter; cake; and chocolate. A second definition was also used, including the 6 major foods introduced in the first 6 months or first 12 months of life: vegetables or fruits; cereals; bread; meat; cake; and yogurt. Children with a low diet diversity, as defined as above, had an increased risk of sensitization to food allergens at age 4.5 or 6 years, but no significant associations were found with sensitization to inhalant allergens. The association remained significant, albeit weaker, in a subgroup analysis of children without food allergy, respiratory disorders or both. Subgroup analysis was carried out to consider the potential risk of reverse causality, given early onset allergy or family history of allergy could lead to low diet diversity due to different feeding practices in those infants. The German LISAPlus study assessed the impact of diet diversity on allergic disease.[109] That study concluded that children in the highest quartile of food group diversity had lower odds of allergic sensitization to aeroallergens. This finding was also supported when food group diversity was treated as a continuous variable. Similarly, in a Finnish birth cohort of over 3,500 children, Nwaru and colleagues[110] studied the association between diet diversity (defined as the number of foods introduced at 3, 4, and 6 months of age) and sensitization to food and aeroallergens at the age of 5 years (see table 3 for definitions used). After adjustment for several demographic and parental factors, they found that reduced diet diversity as early as 3 months was associated with an increased risk of sensitization to specific food and aeroallergens. Whilst the adverse risk estimates became much stronger with increased diet diversity at 4 and 6 months, the authors found that, compared to

non-high-risk children, the at-risk children (i.e. those with atopic eczema by 6 months of age or those with a parental with history of allergy) had a greater risk of allergic sensitization.

Diet diversity and food allergy

Only one study has focused on the potential association of the diversity of food intake and the development of food allergy (table 3). In the aforementioned PASTURE study, Roduit et al.[16] showed that children with a more diverse diet had a lower prevalence of food allergy, measured as a report of a doctor-diagnosed food allergy but not necessarily an allergy proven by oral food challenge. In this study, the inclusion of 0-6 items from vegetables/fruits, cereals, bread, meat, cake, and yogurt within the first 6 months or first year of life, respectively, was recorded. The study showed that children with a low diet diversity score (consumed fewer of the items listed above) had an increased risk of food allergy up to six years of age, compared to children having more food items in their diet.

Diet diversity and atopic dermatitis

A limited number of studies have investigated the association between diversity of complementary food and the risk of atopic dermatitis (AD) in children. In all studies, diet diversity was defined as the sum of the number of complementary foods that were been introduced into the child's diet (even if eaten only once) up to a specified time point, usually within the first year of life. We identified eight unique studies (seven birth cohorts and one matched case-control study), reporting their data in 12 publications originating from Germany, Italy, New Zealand, Finland, Austria, France, and Switzerland (table 4). The pooled data from the GINIPlus and LISA studies revealed that the early introduction of solids with a high diversity before the end of the fourth month was associated with an increased risk of AD at two and six years, but interestingly not at four years.[114] Why this statistical anomaly was seen is not clear, and diversity before four months might be highly influenced by breast/formula feeding practices. Conversely, the delayed introduction of solids and reduced diversity beyond 6 months of age was not beneficial for allergy prevention. Prior to the pooling of the GINIPlus and LISAPlus studies, the LISAplus study reported an increased risk of AD at the age of 2 years associated with less diet diversity at four months of age, but they found no association between diet diversity at four months of life and AD at six years.[111,112] Data from the 15-year follow-up of the LISAplus birth cohort indicated that children in the highest quartile of diet diversity who were introduced to all 8 food groups during the first year of life had lower odds of developing eczema up to age 15 years when compared with children in the lowest quartile.[109]

A birth cohort from New Zealand found that a more diverse diet during the first 4 months of life was associated with an increased risk of developing AD both at 2 and 3 years and an increased risk of recurrent AD at the age of 10 years.[116-119] In this study, diet diversity was defined as the sum of six food groups (cereals, vegetables, dairy products, meat, fruits, egg or related products). The Finnish birth cohort showed that lower diet diversity at six months was associated with an increased risk of AD at 5 years and a same tendency was observed with the diet diversity at 12 months of age.[120] In the European PASTURE study, an increased diet diversity within the 1st year of life was associated with a reduced risk of developing AD through 4 years of age (even after excluding children with AD onset within 1st year of life).[121] This finding was supported by the outcomes from the matched case-control study from Italy, in which the authors reported that more diverse diet at 4 and 5 months was associated with a reduced risk of AD by 2 years of age.[115]

Diet diversity and asthma and allergic rhinitis

Data investigating these relationships were limited to two large European prospective birth cohorts (table 5), the PASTURE study[16] and the Finnish Type I Diabetes Prediction and Prevention Study Prospective Cohort Study.[120] While these cohorts were recruited for different purposes, similar assessment of diet diversity was recorded during the first year of life, as a variable to help predict allergic outcomes at either ages 5 (Finnish Type I Diabetes Prediction and Prevention Study) or 6 (PASTURE). In the PASTURE cohort, Roduit et al.[16] noted that increasing diet diversity in first year of life was associated with a linear protective trend against development of reported asthma, resulting in a 26% reduction for the introduction of each successive food. However no protective association was noted for allergic rhinitis or inhalant sensitization. In the Finnish Type I Diabetes Prediction and Prevention Study, Nwaru et al.[120] noted less diversity at 12 months of life was associated with a greater risk of development of any form of asthma at age 5 for 0-7 foods incorporated in the diet and for 8-9 foods incorporated into the diet compared to > 11 foods ($p<0.001$), as well as increased risk for any wheeze for 0-7 foods vs. > 11 foods ($p=0.004$). For allergic rhinitis, lower diet diversity at both 6 and 12 mo of life was significantly associated with later risk of developing allergic rhinitis. At 6 months, the risk of developing allergic rhinitis was significantly greater with incorporation of 0-4 foods and 5-6 foods vs. >8 foods ($p=0.02$). Similarly, at 12 months the risk was significantly higher with incorporation of 0-7 foods and 8-9 foods vs. > 11 foods ($p<0.001$). (see table 6 for a summary of all allergy outcomes)

Food patterns during infancy and allergy outcomes in the infant

In children, all studies focused on *current* intake vs. allergy outcomes, which does not give an indication of early intake (infancy) vs. later (childhood) outcomes. These studies therefore are not designed to inform us regarding the role of the meditrearrean diet as a proxy measure of diet quality in infancy on allergy outcomes in childhood. Nonetheless, an overview is provided of the mediterrean diet pattern in childhood and its influence on current allergy outcomes. The majority of childhood studies have used either the KIDMED mediterrean score[100,122-127] or the adult EPIC score.[101,128-131] While the KIDMED index reflects what is commonly interpreted as a "healthy and diverse" diet, many Mediterranean diet studies use an index which was developed in a time when saturated fatty acids were believed to increase the risk of cardiovascular disease. Thus, dietary intake is categorized into "pro-Mediterranean diet" (fruit, vegetables, fish, cereals, pasta, rice and potatoes) and "anti-Mediterranean diet" (milk, meat, fast foods). There is however, growing evidence that the "pro-" and "con-"assignment is not only out of date, but that it is not evidence-based, and some of the "anti-Mediterranean diet" foods were actually found to decrease the risk of wheeze/asthma (e.g. meat[98,123,132,133] and milk[99,129,133]).

Mediterranean diet in infancy and childhood

While this is an important relationship to understand, no studies have been identified exploring an association between the Mediterranean diet in infancy and allergy outcomes. Four systematic reviews focussing on nutrients and foods associated with asthma and allergy outcomes investigated the impact of the Mediterranean diet in childhood,[133-136] and found an inverse relationship between eating according to the Mediterranean diet and a range of reported symptoms such as wheeze and asthma. Papamichael et al[135] summarized twelve studies reporting an inverse association between adherence to a Mediterranean dietary pattern and asthma in children. Nurmatov et al. [134] reported that adherence to a Mediterranean diet was protective for persistent wheeze (OR, 0.22; 95% CI, 0.08-0.58) and atopy (OR, 0.55; 95% CI, 0.31-0.97). Garcia-Marcos et al. [133] found a significant negative association between the highest tertile of Mediterranean diet score (OR 0.85, 95% CI 0.75–0.98; p = 0.02) and 'current wheeze'. Lv et al. [136] concluded that the mediterriean diet in children may be associated with prevention of asthma or wheeze, but that randomized controlled trials are required.

Ten original papers were also identified (supplementary table S5) from cross-sectional studies [98,100,122-124,127,129,130,137,138], 3 papers from two (birth) cohorts from Mediterranean regions [100,126,139]; 5 cross-sectional studies from non-Mediterranean regions [101,131,140-142] as well as one paper on using the International Study on Asthma and Allergy in Children (ISAAC) data from 29 centres in 20 countries.[132] These publications focused on a range of allergy outcomes: most of the studies investigated the impact of the Mediterranean diet on risk of wheeze/asthmatic symptoms [100,101,122-128,131-133,138-140,142], sometimes including the development of other allergic outcomes. Only a few studies focussed on atopic dermatitis[129], and allergic rhinitis.[126,130,137] However, as with the maternal studies, none of the studies focused on food allergy as an outcome.

The majority of studies used FFQs completed by parents[101,122,125,127,129] and semi-quantitative questionnaires[100,123,126,130,131] to calculate either the KIDMED index[122-127] or another index to assess adherence to a Mediterranean diet.[138] The analysis of the ISAAC study[132] assessed adherence to a Mediterranean type diet using their own food categorization. Selected food items with either positive (+) or negative scoring (-) included were meat (-), fish (+), fresh fruit (+), raw green vegs (+), cooked green vegs (+), burgers (-), fruit juice (+), fizzy drinks (-).

Adherence to the Mediterranean diet was primarily evaluated by using two different indices. While the KIDMED index, used in 6 studies [122-127], reflects what is commonly interpreted as a "healthy and diverse" diet, the other Mediterranean diet studies used the EPIC index[101,128-131] (developed by Psaltopoulou/Trichopoulou[94,143]). The EPIC score allowed a total of 10 points from incorporation of the following foods into the diet: Vegetables, Legumes, Fruit, Dairy products, Cereals, Meat and meat products, Fish and seafood, Olive oil, Monounsaturated: Saturated lipids, and alcohol intake.

Summarizing the available data on the association between the Mediterranean diet and childhood allergy outcomes is difficult, primarily due to different definitions of the Mediterranean diet and allergy outcomes assessed. Some studies showed a small but positive effect on current severe asthma in girls[137] and a protective effect on asthma/wheeze. [101,128,132,142] Alternatively, some studies showed no protective effect on asthma and/or rhinitis symptoms[130,131,140,141] or atopic dermatitis.[129] None of the studies reported on food allergy as an outcome.

Other dietary patterns in infants and childhood allergy outcomes

Dietary patterns other than the Mediterranean diet were also studied in children. Three birth cohorts were identified [144-147], two cross-sectional in design[37,38] and 3 papers on a case-control study within a

cohort.[148-150] Some of the identified publications on the Mediterranean diet also studied other dietary patterns.[123-126,129-131] Dietary intake was assessed using FFQs.[37,38,105], 24 hour recalls[145], semi-quantitative questionnaires,[144] and prospective food diaries.[148-150] (supplementary table S5).

Two studies showed that food intake relating to a Western dietary pattern was associated with an increased prevalence of wheeze/asthma.[37,38] A study from Singapore identified the pattern "noodles and seafood" as protective against the development of allergen sensation in Asian infants in the second half of the first year of life. [147] Grimshaw et al.[148-150] found that a diet pattern obtained from Principal Component Analysis on prospective food diary data described as "predominantly home cooked" (fruit, vegetable, fish, and poultry consumption) in UK infants was associated with a reduced prevalence of food allergy. In contrast to other studies, analysis of the dietary data of the Dutch Generation R cohort did not find that a healthy dietary pattern in early life is associated with a lower risk of allergic sensitization or atopic diseases in childhood.[144]

Key measurement issues to address when designing studies assessing the association between diet diversity and allergy outcomes

Research into diet diversity should have 3 particular prerequisites; 1) the method used needs to be specific to the outcome which may include nutritional intake, growth or health outcomes; 2) the diet diversity tool needs to be able to measure food security and socio-economic status[151,152]. This needs further clarification as well as careful statistical guidance to disentangle the impact of socio-economic status vs. diet diversity on outcomes; and 3) consideration should be given to healthy diet diversity vs. unhealthy diet diversity when studying disease outcomes to inform diet recommendations. Researchers must consider that diversity in diets are also strongly related to local and ethnic traditions, with regional environmental exposures leading to unmeasured/unmeasurable characteristics which could potentially impact on short-, medium-, and long-term outcomes. These considerations will apply to the most studied model of diet intake, that is, the Mediterranean diet, which partly explains some "caveats" within previous paragraphs.

Delphi Consensus

The EAACI task force agreed that the systematic review was unable to answer a number of key questions. . Given the complexities and confusion/inconsistencies of the concept and terminology in the existing literature for diet diversity, the organizing members of this taskforce initiated methods to

provide an expert consensus regarding multiple concepts, in order to provide a pathway forward for future research into diet diversity and allergic outcomes. In the absence of established clinical trials or observational research studies with agreed definitions and nomenclature, expert opinion obtained in this fashion becomes an acceptable alternative. [66,153-155] The panel used the modified Delphi Method (written questionnaire was not used) technique to reach consensus on outstanding issues identified in these literature searches regarding diet diversity in relation to various allergic outcomes. A single-group, single-round method was chosen for developing consensus on all statements. Feedback was given on each statement. Questions were written by 4 committee members based on identified gaps in each subsection in this document, and refined in an iterative manner among these individuals (CV, LM, RM, MG) until there was consensus, and then the questions were formatted into an electronic survey software (RedCAP) and emailed to the group. Responses were gathered over a 2-week period of time, then tallied and discussed among the wider group. The tally was then either confirmed or revised based on panel member insights from the discussion. Consensus threshold was defined a priori as agreement on a given statement by 75% of the committee members. This threshold was chosen based on existing literature and agreed upon as an appropriate level by the experts. The questions, vote tally, and final responses are summarized in table 7, and the final recommendations noted in table 1. Threshold for consensus was set at 18 votes in favour of the statement (75% of the 24 panel members).

Conclusion

We have performed a systematic review particularly investigate the association between diet diversity and allergy outcomes in infancy and childhood. Currently, we suggest that diet diversity in infancy may be associated with reduced allergy outcomes, but additional studies are required to define more clearly the role of diet diversity and diet patterns, whilst clearly adjusting for appropriated confounders. There is no data on diet diversity in pregnancy and allergy outcomes in the offspring. Data on diet quality in pregnancy is not consistent, but usually indicates an inverse association with asthma/wheeze in the offspring. There is no data on diet quality in infancy, but studies in childhood, show a possible association with reduction in wheeze/asthma and perhaps food allergy. These conclusions have to be interpreted taking into account that previous studies using different defintions of diet diversity, and different instruments to measure diet diversity.

In line with the European Food Safety Authority (EFSA)[156], we endorse a " complementary approach to traditional monitoring and surveillance programs of dietary intake, which instead of focusing on compliance is designed to provide a solid basis for calculating population dietary exposure and assessing potential impact on public health. Harmonizing the total diet study methodology, focused on specifically allergy outcomes, will enhance the value of these programs by improving the comparability at international level".

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Table 1: Factors to consider when measuring diet diversity to improve the validity and reliability of diet diversity measured:

	Current state of knowledge	Recommendations regarding measuring diet diversity based on current literature	Practice points regarding measuring diet diversity based on Delphi consensus from the EAACI task force: Voting: >80% agreement
Definitions	See box 1	Diet Diversity, Diet Quality and Diet Patterns are distinct entities of food intake and these terms should not be used interchangeably.	In future, there may be an index that better describes the allergenic potential of foods or food patterns within the context of diet diversity better.
In order to measure diet diversity			
Population studied	The majority of studies on diet diversity have been carried out in children. The tool used should take into account measurements in developed vs. developing countries.[1,28]	- The age group studied must be clearly specified. - The diet diversity tool should preferably be validated in that age group, and sociodemographic information should also be collected. - The diet diversity tools required may be different depending on the populations studied	
Food vs. food group	It is unclear if foods, food groups or both best describes diet diversity since some studies favour foods, others favour food groups or favour both. [29-32]	- Either foods or food groups can be studied to measure diet diversity. - Foods and/or food groups that are studied should be clearly specified and identifiable e.g. fresh fruit vs. fruit juice	Diet diversity scores should be weighted depending on the types of food being measured (e.g. a diverse fast food diet is not equal to a diverse fruit and vegetable diet). Diversity scores should be weighted depending on the types of food being measured (e.g. a diverse fast food diet is not equal to a diverse fruit and veg diet).
Defining food groups	Food group selection and whether these foods groups should be selected based on their nutritional value. This decision should be dependent on the outcome being studied e.g. nutritional intake, food security or disease outcome. [1,28] Allergen intake has been used as a marker for diet diversity.[33] The study found no consistent association between timing and diversity of allergenic solid food introduction and allergic sensitization, physician-diagnosed food allergy or eczema up to 10 years of age. "Food biodiversity is defined as the diversity of plants, animals and other organisms used as food, covering the genetic resources within species, between species and provided by ecosystems" Food biodiversity therefore measures food intake based on their scientific classifications and may be useful to determine nutritional intake[34]	- Food groups chosen should be selected based on the outcome to be studied	Diversity of intake of specific foods e.g. range of fruits eaten, different types of cheese consumed, different types of home-cooked or processed foods cannot be used to describe diet diversity but the terms "diversity of fruit intake", "diversity of cheese intake", or "diversity of processed food intake" can be used. These foods can however be included in combination with other foods to determine overall diet diversity. For allergy (asthma, food allergy, eczema, rhinitis, allergic sensitization), there is the opportunity to measure allergenic food diversity, which relates to the number and/or amount of food allergens introduced in a given period of time, e.g. the first year of life. It is important to understand that allergenic food diversity may not reflect diet diversity, as an emphasis on allergenic food intake may lead to an overall reduced diet diversity. There is the opportunity to measure food biodiversity, which relates to the taxonomic classification of food intake e.g. classifying tomatoes as Solanum (genus) opposed to vegetables.

	Microbial diversity of food: Studying foods with a high biodiversity of microbial content such as unpasteurised milk (atopic dermatitis and atopiy) [35]and fermented foods such as cheese or yoghurt (food allergy and atopic dermatitis)[36] as an indicator of intake of microbial diversity, and a source of short chain fatty acids, gives an indication that these foods may be associated with allergy prevention. Studies focusing on westernized diets[37-39] (also high in advanced glycation end products, soda, fruit juice[40,41], cured meats[42] and fast food[43]) suggest that increased intake of AGEs is associated with reduced diet diversity and increased allergy outcomes. A number of studies have indicated that certain nutrients (e.g. antioxidants) of foods (fruit and vegetables or fish) may have a beneficial effect on prevention particularly of infant wheeze[44-46] [47] or eczema in the infant.[48] [46]		There is the opportunity to measure food microbial diversity which relates to the microbial content of foods. Diversity of intake of foods containing specific nutrients or ingredients e.g. foods containing advanced glycation end products or foods containing omega-3 fatty acids cannot be used to describe diet diversity but the terms "diversity of advanced glycation end products intake" or "diversity of foods containing omega-3 fatty acid intake" can be used. These foods can however be included in combination with other foods to determine overall diet diversity. In these instances, diversity may have a positive (fruit and vegetables) or a negative (advanced glycation end products) connotation. This list may continue to grow as we gain more knowledge about foods/nutrients with immunomodulatory potential e.g. bovine trans fatty acids which are isomers of linoleic acid.[49]
Portion size	It is unclear if portion size should be included when measuring diet diversity and it will depend on the outcome being studied. Two points are of particular importance: [1,28,50] - Should portion size be included to better describe nutritional intake - What is the minimum portion size to include as including foods eaten in small amounts (<15 g of the food) can falsely inflate diet diversity, particularly if nutritional intake is being studied	Portion size should be defined and measured using quantitative or semi-quantitative questionnaires when required to describe diet diversity.	It is not possible at present to define the minimum amount of allergenic protein that should be consumed in order to be sufficient within the allergenic food diversity measure.
Frequency of intake	Whether frequency of intake should be measured, will depend on the question asked [1,28,50]	- Frequency of specific food or food group exposures should be measured in diet diversity studies.	
Scoring system	For simple diet diversity, the number of foods or food groups consumed over a given time is usually stated. Weighted scores can be assigned to indicate how often a food or food groups were consumed over a given period of time. More complex scoring systems that include more detailed information such as the number of portions or portion size, usually forms part of a dietary index as opposed to indicating diet diversity.[51-53]	- Scoring systems for diet diversity are simple and measure the number of foods or food groups consumed over a given timeframe.	
Cut off values	It is difficult to define what constitutes high or low diversity of foods or food groups and cut-off points	- Cut-off values of high/low diversity can only be correctly ascertained at a population level, where the sample is	When possible, studies reporting diet diversity data should include sensitivity, specificity, true and false

	should be determined in the context of why and in which population the diet diversity is measured. In terms of determining nutrient adequacy, it is recommended that cut-offs should take local food systems and dietary patterns into account. In some instances, sensitivity-specificity analysis[29] or receiver-operating characteristics (ROC) curves[54] can be used to determine cut-off points.	robust and representative of the population to allow generalizability. Consequently, these may differ in different populations.	positive/negative values to assist future meta-analyses and comparisons. They should also de-emphasize reporting of a cut-off value for a sample
Recall period	The optimal recall period required to assess dietary diversity will depend on daily variety of intake, risk of recall errors, and for intake data can be used at individual or population level. - On an individual level, the number of foods being eaten reaches a plateau after 10-15 days.[55] In addition, as the curve increases steeply for the first 3 days, measuring diet diversity based on a 1-day recall may underestimate dietary diversity. - On a household or population level, the reference period is still unclear, but seems to be shorter than measuring nutrient intake at an individual level. - Ultimately, the number of days included in the recall period should take participant burden and feasibility into account.[1,56-58]	- The recall period and method of data collection should be clearly specified, but age of introduction for each food during infancy should also be reported given this may have a potential significant confounding effect.	For pregnant women, we recommend a minimum recall period of 2 week days and 1 weekend day (**i.e. 3 days**), measured at repeated intervals throughout pregnancy. When possible, portion sizes should be collected and reported. For infants, we recommend food recall periods within the first year of life. These periods may include the first four months of life, the first six months of life or the first year of life. Repeated measure of intake is recommended to improve the quality of data, rather than just recording consumption of a particular food/food group once. When possible, portion sizes should be collected and reported and data should ideally be recorded prospectively. .
Primary source of food procurement and food preparation	Information about the primary source of food procurement may be important to determine intake of either for the whole or certain specified foods/food groups (fruit, vegetables, dairy) e.g.[50] 1= Own production, gathering, hunting, fishing 2= Purchased 3= Borrowed, bartered, exchanged for labor, gift from friends or relatives 4= Food aid 5= Other Food preparation can also affect the microbial content of food. Food preparation can therefore potentially affect the allergy preventative potential of foods.[59 9,60-62]	- Investigators should consider ways to ensure measuring food procurement in their study design, and if/when possible, this should be detailed for both diet diversity and diet quality.	Investigators should consider ways to ensure measuring how food is prepared/cooked (e.g. Raw, home cooked, processed, ultra processed and fermented) is recorded in their study design, and if/when possible, this should be detailed for diet diversity. Ideally, foods should be defined as raw, home-cooked, processed or ultra-processed.
Consumption of Fortified foods	If digestion of fortified foods is important for the outcome studied, then the questionnaire may need to address this or at least consider the local availability of these.[28,50]	- If fortified foods are consumed, the study should aim to capture this data, and the amount quantified. - If any vitamin or mineral or nutritional supplements is consumed in the study, this should be reported, including brand and the amount consumed. Detail of probiotic and prebiotic supplements should also be recorded. Foods already supplemented with any of the above should also be clearly recorded.	
Mixed dishes or foods with multiple ingredients	As with foods consumed in small amounts, it is important to err on the side of caution and not inflate what was eaten. [28,50]	- If mixed dishes are consumed, this should be clearly specified, and the method for how individual food or allergen content quantification was achieved should be fully detailed for both diet quality and diet diversity	
Open recall methods	There is anecdotal evidence that predefined lists of	- Open recall e.g. 24 hour recall is the preferred method	

or predefined list of food	food eaten may collect less complete information than when food intake is determined in an open/unstructured fashion. [28,50]	of ascertaining foods or diet quality index. Pre-defined lists are less preferable, but if used, these should be clearly defined in the methods or in a supplemental file.	
Age of weaning and introduction of infant formula	Data suggest that age of introduction of solid foods[63], food allergens[24,25] and infant formula[64] may affect allergy outcomes. Introduction of solid foods during the weaning period increase the diversity of the gut microbiome[18]		Age of introduction of solid foods, allergenic foods and infant formula should be clearly indicated in studies investigating the association between diet diversity and allergy outcomes Introduction of infant formula cannot be classified on its own as diet diversity but should be included in measuring diet diversity of food and food groups. Introduction of infant formula may in fact reduce diet diversity as breast milk potentially exposes an infant to the diversity of the maternal diet, whereas formula is uniform.
Other factors that may affect allergy outcomes	Studies looking at growth, nutritional intake and health outcomes other than allergic diseases, do not need to control for other risk factors of allergic diseases, but these will need to be controlled for in diet diversity studies.[65]	There is a non-exhaustive list of factors that may affect allergy outcomes, but potential confounders should be corrected for analyzing associations between diet diversity and allergy outcomes.	

Table 2: The association between diet diversity and sensitisation to food and aero-allergens

Study and country	Definition and assessment of diet diversity	Results	Comments
Roduit C et al. 2014[16] Prospective birth cohort study Protection Against Allergy Study in Rural Environments (PASTURE/EFRAIM). Stratified in farm and non-farm children Sample Size: Baseline N: 1133 Analytic N: 856 Attrition: 75% Sex: 49.5 % girls and 50.5% boys Race/Ethnicity: Rural areas of 5 European countries (Austria, Finland, France, Germany, and Switzerland. Atopic Disease Risk Status: 53.6% had at least 1 allergic parent Background Diet: 47.4% were breastfed for more than 6 months (not exclusively)	Intervention/Exposure: Parental administered questionnaires for asthma, rhinitis and food allergy within the third trimester of pregnancy and when the children were 2, 12, 18, and 24 months of age and then yearly up to age 6 years Asthma: at least one either doctor-diagnosed asthma or at least 2 doctor-diagnosed episodes of obstructive bronchitis in the last 12 months in the year 4, 5, or 6 questionnaires independent of a diagnosis reported in the first 3 years of life. Food allergy: at least once been given a diagnosis of food allergy by a doctor up to age 6 years. Allergic rhinitis: Reported presence of symptoms (itchy, runny, or blocked nose without a cold and associated with red itchy eyes) or doctor-diagnosed allergic rhinitis in the 6-year questionnaire. DD was assessed through food items in monthly food diaries from 3rd -12th months. DD scores were calculated as follows: (1) using major food items introduced in the first year of life (including vegetables or fruits, cereals, bread, meat, cake, and yogurt); (2) with the same major food items but introduced in the first 6 months of life; and (3) with all food items introduced in the first year of life	Complementary food introduction associated with asthma, food allergy, allergic rhinitis, and atopic sensitisation up to 6 years of age Assessment Methods: DD score and parent reported asthma, rhinitis and food allergy. Specific IgE levels to indicate sensitisation Results Sensitisation to any allergen at age 4.5 and/or 6 years was present in 25.5% of children, sensitisation to food allergens was present 10.7%, and sensitisation to inhalant allergens was present in 22.1%, as measured at 4.5 or 6 years. Increased DD within the first year of life was negatively associated with sensitisation to food allergens at 4.5 or 6 years of age. The children with a low DD had an increased risk of sensitisation to food allergens at age 4.5 or 6 years. The analysis with children having doctor-diagnosed food allergy combined with positive food sensitisation showed an even stronger negative association with DD (adjusted OR for each additional food items: 0.55, 95%CI: 0.40-0.76). Children with a low DD, had an increased expression of marker for antibody isotype switching to IgE and a reduced expression of the regulatory T cell–associated gene Foxp3 measured at 6 years of age.	Confounders: Confounders adjusted for in this publication. (in particular atopic dermatitis) Limitations: - Study population were selected from rural Europe and may not reflect general population. - Outcomes of asthma, food allergy and rhinitis were based on parental reports. - Reverse causality can not be ruled out in this study - DD score used was not validated and made use of allergens and foods like chocolate and margarine as part of the diversity score, which may not be representative of true DD.

	(including any cow's milk, yogurt, other milk product, eggs, nuts, vegetables or fruits, cereals, bread, meat, fish, soy, margarine, butter, cake, and chocolate) Assessment Methods: parent self-administered questionnaire on dietary intake. Levels of allergen-specific IgE antibodies (Dermatophagoides pteronyssius, Dermatophagoides farinae, alder, birch, hazel, grass pollen, rye, mugwort, plantain, cat, horse, dog, Alternaria species, hen's egg, cow's milk, peanut, hazelnut, carrot, and wheat flour) were measured in blood among children at age 4.5 and 6 years. Sensitisation was defined as ≥ 3.5 kU/L Assessment of DD age: at 6 and 12 months of age		
Markevych I et al. 2017[109] Population-based German birth cohort LISAplus (Influences of Lifestyle related Factors on the Immune System and the Development of Allergies in Childhood) Sample Size: Baseline N: 3097 Analytic N: 2518 Attrition: 81% Sex: See original LISAPlus study	Intervention/Exposure: Impact of DD within the first 6 months of life on 5 allergic outcomes: doctor-diagnosed eczema, asthma and allergic rhinitis and sensitisation to aeroallergens and food allergens. Assessment Methods: Self administered biannual parental questionnaires on the children's health and on lifestyle factors from birth to 2 y and at 4 y and 6 y. Blood samples for specific IgE at 2 and 6 y, levels > 0.35 KU/L were defined as sensitisation. At 12 months of age, parents were asked	Allergic outcomes at 2 and 6 and 15 years of life Assessment Methods: Several definitions of DD (food group and food item diversity, each treated in quartiles and continuously) during the first year of life. All analyses were stratified by the presence of a wide range of early skin symptoms to test the impact of reverse causality. Allergic outcomes were assessed at 6, 12, and 18 months and age 2,4, 6, 10, and 15 years. Results Children in the highest quartile of food group diversity had lower odds 0.61 (0.44-0.85) of	Confounders: Confounders adjusted for: atopic eczema Limitations: - Information on frequency and amount of food intake not available. - Reverse causality could not completely be ruled out - DD score used not validated

Race/Ethnicity: See original LISAPlus study Atopic Disease Risk Status: 57.2% had atopic family history	about breastfeeding practices and about the timing of solid-food introduction. Possible answer choices included: "1st until 4th month," "5th/6th month," "7th to 12th month," and "solid food item not yet introduced." Forty-eight food items were grouped into 8 food groups: (1) vegetables(avocado, cauliflower, beans, broccoli, peas, cucumbers, carrots, potatoes, white cabbage, turnip, cabbage, lenses, celery, asparagus, spinach, tomatoes, onion, vegetable juices); (2) fruit (apples, pineapples, apricots, bananas, pears, strawberries, peaches, citrus fruit, fruit juices); (3) cereal (bread/pretzels/rolls, cookies/cakes/rusk, rolled oats, muesli, millet, cornmeal/corn starch, wheat semolina/starch, noodles, rice/rice starch, spelt); (4) meat (poultry, lamb, veal/beef, pork, sausages); (5) egg; (6) dairy products (cow milk/cream, yoghurt/quark/cheese); (7) fish; and (8) other (nuts, soy products, cocoa/ chocolate). Assessment of DD age: DD at 6 months and 12 months of age	allergic sensitisation to aeroallergens. When food group diversity was treated as a continuous variable, those with a higher DD had statistically significantly less allergic sensitisation to aeroallergens in the total population and in children with early skin symptoms. 0.88 (-0.80 - 0.95) When food item diversity was used as an exposure variable instead of food group diversity, similar associations for allergic sensitisation to aeroallergens were observed. Highest quartile 0.82 (0.52 - 0.98); Continuous variable 0.99 (0.97 – 1.00)	
Nwaru B et al. 2013[110] Finnish Type 1 Diabetes Prediction and Prevention study Prospective Cohort Study Finland Sample Size:	Intervention/Exposure: The child's diet was assessed by using age-specific dietary questionnaires at ages 3, 4, 6, and 12 months and a follow-up ''age at introduction of new foods'' form for recording the age at introduction of complementary foods. Looked at: the number of complementary foods introduced at 3, 4, and 6 months of age. 4 categories of food diversity at each time point were defined based on the	Sensitisation to the following food and aeroallergens were analysed at the age of 5 years: egg, cow's milk, fish, wheat, house dust mite, cat, timothy grass, and birch. These outcomes were based on analysis of IgE concentration using ImmunoCAP fluoroenzyme immunoassay. Atopic sensitisation was defined as IgE ≥0.35 kU/l. Less DD as early as 3 months was associated with an increased risk of allergic sensitisation	Confounders: Confounders adjusted for: sex of the child, number of siblings, parental asthma, parental rhinitis, delivery hospital, and maternal smoking during pregnancy. Limitations: - The study recruited children carrying genetic

Baseline N: 4074 Analytic N: 3781 Attrition: 93% Sex: 1646 boys (52%), 1496 (48%) girls Race/Ethnicity: not mentioned Atopic Disease Risk Status: 16% and 62% of parents had asthma and rhinitis respectively	distribution of the data at each time point: at 3 months, these were ‘‘no food item,’’ ‘‘1-2 food items,’’ and ‘‘>2 food items’’; at 4 months, these were ‘‘no food item,’’ ‘‘1-2 food items,’’ ‘‘3-4 food items,’’ and ‘‘>4 food items’’; at 6 months, these were ‘‘0-4 food items,’’ ‘‘5-6 food items,’’ ‘‘7-8 food items,’’ and ‘‘>8 food items’’; Food groups used as DD definition: cow’s milk and formula (as a combined variable); potatoes; carrots; turnip; fruits and berries (as a combined variable); cereals (rye, wheat, oats, and barley as a combined variable); other cereals (maize, rice, millet, and buckwheat as a combined variable), meat; fish; egg; cabbage; spinach; and lettuce. Assessment Methods: Prospective Parent questionnaires Assessment of DD age: birth to 12 months of age	at 5 years. The associations were stronger with DD at 4 and 6 months and more prominent in at-risk children compared to no-high-risk children. Less DD as early as 3 months was associated with an increased risk of allergic sensitisation at 5 years. Food Allergen sensitisation[110]: No food at 3 months vs >3 foods 1.39 (1.07 – 1.81); 1-2 foods at 3 months vs >3 foods 1.36 (1.06 – 1.74) p value 0.021	risk (HLA-conferred susceptibility) for type 1 diabetes. Therefore, may reduce generalizability of findings to general population - The number of statistical tests performed could mean that the type 1 error rate might not be at the 0.05 level. DD definition was not validated and could be improved with increasing the variety

Table 3 The association between diet diversity and food allergy

Study and country	Definition and assessment of diet diversity	Results	Comments
Roduit C et al. JACI 2014[16] Prospective birth cohort study Protection Against Allergy Study in Rural Environments (PASTURE/EFRAIM). Stratified in farm and non-farm children See – food sensitisation	See – food sensitisation	Food allergy: parental report of ever doctor-diagnosed food allergy up to 6 years of life (overall proportion: 7.4%). Food diversity score (0-6 items): - 0-3: FA 21.9% - 4-5: FA 9.2% - 6: FA 5.7% Food diversity score (0-6 items): - 0-3: food sens. 26.9% - 4-5: food sens. 13.1% - 6: food sens. 8.5% Increased diet diversity in the 1st year of life: reduced risk of reported doctor-diagnosed food allergy up to 6 years (adjusted OR for each additional food items: 0.70, 95%CI: 0.57-0.86) and food sensitisation at 4.5/6y (adjusted OR for each additional food items: 0.72, 95%CI: 0.57-0.90).	Outcome assessment mainly based on parental reports of doctor-diagnosis. Adjustment for the potential confounders was performed: farmer, centre, duration of breast-feeding, parents with allergy, maternal education, sex, and number of siblings. Reverse causality was taken into account to some extent, i.e. - - - analysis with exclusion of children with FA within the 1st year of life - analysis with exclusion of children with AD within the 1st year of age. However did not account for lactose/food intolerances as lack of information and also lack of information on subclinical manifestations of food allergy (colic, gastroesophageal reflux etc)

Table 4: The association between diet diversity and atopic dermatitis

Study and country	Definition and assessment of diet diversity	Results	Comments
Zutavern A et al. Pediatrics 2006[111] Zutavern A et al. Pediatrics 2008[112] Germany LISA study N=2612 up to 2 years LISA study N=2073 up to 6 years	Solids diversity was defined by the total number of different food groups (48 single food items were asked in a questionnaire) and classified in 8 groups of solid food: vegetables, cereal, fruit, meat, dairy products, egg, fish and others (like soybean, nuts, cacao, chocolate) introduced in the child's diet at 4 and 6 months of age Assessment method: parental interview on infant's diet at 6 months and parental interview on infant's diet at 12 months	Assessment of AD: parental reports on doctor-diagnosis and symptoms of AD, questionnaires at birth, 0.5, 1, 1.5, 2, 4, and 6 years Introduction of a high number of different solid foods by 6 months of age reduced the risk for doctor diagnosed AD up to 2 years in all children (aOR 5-8 food groups versus no solid food: 0.66, 95%CI: 0.46-0.94) and also in the children having early skin or allergic symptoms Increased diet diversity within first 6 months: reduced risk of AD at 2 years (no significant association with DD at 4 months and AD) No association between diet diversity at 4 months and AD at 6 years, for all population. Exclusion of children with early skin or allergic symptoms: increased DD was associated with an increased risk of doctor-diagnosis of AD, but not symptoms of AD at 6 years	Families with higher educational background and high proportion of atopic parents were included. Reverse causality was taken into account: separate analysis with AD children with and without early skin symptoms Confounding factors due to the children included in the analysis; recall bias due to retrospective information regarding introduction of solids – misclassification of feeding history possible; Information on eczema from questionnaire
Filipiak B et al. J Pediatrics 2007[113] Germany GINI study N=4753	Solids diversity was defined by the total number of different food groups (48 single food items were asked in a questionnaire) and classified in 8 groups of solid food (vegetables, cereal, fruit meat, dairy products egg, fish, others like soybean, nuts,	Assessment of AD: parental reports on doctor-diagnosis and symptoms of AD, yearly up to 4 years No association between doctor	Selection bias due to loss of follow up (non-intervention subgroup 25%, intervention subgroup 14%); Misclassification due to recall bias (exposure was assessed retrospectively at 1 year of age)

	cacao, chocolate) introduced in the child's diet at 4 and 6 months of age Assessment method: parental interview on infant's diet at 12 months	diagnosed or symptomatic AD and time-point of solid food introduction and diversity of solids Intervention group: family history of allergy, prospectively and randomly assigned to either hydrolyzed formula or cow's milk formula; Non-intervention group: no family history of allergy or parents did not wish to participate in intervention trial No association between diet diversity at 4 or 6 months and AD up to 4 years	
Sausenthaler S et al. Am J Clin Nutr 2011[114] Germany GINIplus and LISA plus study	Solids diversity was defined by the total number of different food groups (48 single food items were asked in a questionnaire) and classified in 8 groups of solid food (vegetables, cereal, fruit meat, dairy products egg, fish, others like soybean, nuts, cacao, chocolate) introduced in the child's diet at 4 and 6 months of age; high diversity of solid foods: 3-8 groups Assessment method: parental report	Assessment of AD: LISA study: parental reports on doctor-diagnosis and symptoms of AD, up to 4 years in GINI study and up to 6 years in LISA study No association between diversity of solid foods at the age of 4 months and 6 months and doctor-diagnosed AD during first 4 years of life. At 6 years of age significant association between AD and high diversity of solid foods. Symptomatic eczema at 2 years of age was associated with high diversity of diet at 4 mo → conclusion: early introduction of solid foods and high diversity before 17 weeks of age may increase allergy risk.	Reverse causation was not controlled for as in the GINIplus study early symptoms of eczema was not assessed; results on association between high diversity of solids in infants within the first 4 months and increased risk of eczema was not consistent throughout different outcome measures and different time-points.

		Increased diet diversity at 4 months: associated with increased risk of symptoms of AD at 2 years and doctor-diagnosed AD at 6 years, but not at 4 years	
Markevych I et al. 2017[109] Population-based German birth cohort LISAplus (Influences of Lifestyle related Factors on the Immune System and the Development of Allergies in Childhood) Sample Size: Baseline N: 3097 Analytic N: 2518 Attrition: 81% Sex: See original LISAPlus study Race/Ethnicity: See original LISAPlus study Atopic Disease Risk Status: 57.2% had atopic family history	Intervention/Exposure: Impact of DD within the first 6 months of life on 5 allergic outcomes: doctor-diagnosed eczema, asthma and allergic rhinitis and sensitisation to aeroallergens and food allergens. Assessment Methods: Self administered biannual parental questionnaires on the children's health and on lifestyle factors from birth to 2 y and at 4 y and 6 y. Blood samples for specific IgE at 2 and 6 y, levels > 0.35 KU/L were defined as sensitisation. At 12 months of age, parents were asked about breastfeeding practices and about the timing of solid-food introduction. Possible answer choices included: "1st until 4th month," "5th/6th month," "7th to 12th month," and "solid food item not yet introduced." Forty-eight food items were grouped into 8 food groups: (1) vegetables(avocado, cauliflower, beans, broccoli, peas, cucumbers, carrots, potatoes, white cabbage, turnip, cabbage, lenses, celery, asparagus, spinach, tomatoes,onion, vegetable juices); (2) fruit (apples, pineapples,	**Allergic outcomes at 2 and 6 and 15 years of life** **Assessment Methods**: Several definitions of DD (food group and food item diversity, each treated in quartiles and continuously) during the first year of life. All analyses were stratified by the presence of a wide range of early skin symptoms to test the impact of reverse causality. Allergic outcomes were assessed at 6, 12, and 18 months and age 2,4, 6, 10, and 15 years. **Results** Children in the highest quartile who were introduced to all 8 food groups during the first year of life had lower odds of developing eczema up to age 15 years compared with children in the lowest quartile with a maximum of 5 food groups. When food group diversity was treated as a continuous variable, those with a higher DD had statistically significantly less eczema.	**Confounders:** Confounders adjusted for: atopic eczema **Limitations:** - Information on frequency and amount of food intake not available. - Reverse causality could not completely be ruled out - DD score used not validated

	apricots, bananas, pears, strawberries, peaches, citrus fruit, fruit juices); (3) cereal (bread/pretzels/rolls, cookies/cakes/rusk, rolled oats, muesli, millet, cornmeal/corn starch, wheat semolina/starch, noodles, rice/rice starch, spelt); (4) meat (poultry, lamb, veal/beef, pork, sausages); (5) egg; (6) dairy products (cow milk/cream, yoghurt/quark/cheese); (7) fish; and (8) other (nuts, soy products, cocoa/ chocolate). Assessment of DD age: DD at 6 months and 12 months of age		
Turati F et al. Allergy 2016[115] Italy Matched case control study on incident physician-diagnosed AD (451 cases and 451 controls)	The total number of food items included in the infant's diet at 4 and 5 months of age; no solids, 1-2 foods, 3-22 foods Assessment method: face to face questionnaire	Diagnosis of AD by dermatologist, at the age of 3-24 months Weaning at age 4 -5 months was inversely associated with AD risk. Introduction of a high number of different solid foods at 4 and 5 months was associated with a reduced risk of AD (OR: 0.30, 95% CI: 0.11-0.81 ≥3 foods vs 0 foods at 4 months; OR: 0.44, 95% CI:0.21-0.91 ≥ 8 foods vs 0 foods at 5 months)	Maternal recall bias, reverse causation by prolonged exclusive breastfeeding due to mothers considering children at risk for allergies; lack of information on maternal diet during pregnancy and lactation.
Fergusson D et al. 1981[116] New Zealand Baseline N: 1265 Analytic N: 1156 Atopic Disease Risk Status:	Diet diversity assess at 4months: Food groups used as DD definition: cereals, vegetables, dairy products, meat, fruits, egg or related products, other solid foods Food groups categorized as: 0, 1-2, 3-4, 5+	Atopic Dermatitis assessed at 2 years. Assessment Methods: Maternal report; some with physician follow-up Increased diet diversity at 4mo was associated with increased eczema at 2years (0 food groups: 13%; 1-2 food groups: 17%; 3-4	Adjusted for: Parental history of allergic disease **Limitations:** No info on similarity of groups at baseline. No blinded/validated assessments of outcome. Key confounders not taken into accound (education, SES, sex, race/ethnicity, feeding practices, birth size,

24% parental history of atopy Background Diet: 19% exclusively breast fed at 4 months	Assessment methods: Parent interview and food diary	food groups: 17%; 5+food groups: 33%; P<0.05) Increased diet diversity at 4mo was associated with an increaserd risk for AD at 2years	gestational age, smoking, pets) Timing of DD assessment (most children don't eat by 4 months)
Fergusson et al. J Epidemiol Community Health 1982[117] New Zealand Birth cohort of New Zealand N=1143	Diet diversity assess at 4months: DD definition: sum of food groups (cereals, vegetables, dairy products, meat, fruits, egg or related products), which the child had been given during the first 4 months. Categorized as follows: 0, 1-3, 4+ food groups Assessment method: Parent interview and food diary	Atopic Dermatitis: maternal report or directly from the child's doctor information on doctor-diagnosis of AD, up to 3 years Increased diet diversity within the first 4 months of age: increased risk of AD up to 3 years (proportion of AD by numbers of solid food: 0: 18.4%; 1-3: 20.6%; 4+: 24.3%)	Adjusted for parental AD and/or asthma, infant milk diet. Analyses stratified depending on infant milk diet (breastfeeding, bottle only, or both)
Fergusson D et al. Pediatrics 1990[118] New Zealand Birth cohort of New Zealand N=1067	Diet diversity assess at 4months: DD definition: sum of food groups (cereals, vegetables, dairy products, meat, fruits, egg or related products), which the child had been given during the first 4 months. Categorized as follows: 0, 1-3, 4+ food groups Assessment method: Parent interview and food diary	Atopic Dermatitis: maternal report on doctor-diagnosis of AD, up to 10 years of age (31% at least once report of medical attendance for AD). Definition of a sub-group with recurrent or chronic AD (at least 3 medical visit for AD, condition has lasted at least 3 consecutive years and regular treatment for AD) (7.5%) Increased diet diversity within the first 4 months of age: increased risk of recurrent/chronic AD up to 10 years (2.9 times increased risk: 4+ food groups versus no foods)	Adjusted for age at onset of AD, parental and siblings history of allergy, SES, maternal education, age of mother, ethnic status, breastfeeding,
Fergusson D et al. PAI 1994[119]	Diet diversity assess at 4months: DD definition: sum of food groups	Atopic Dermatitis: maternal report or directly from the child's doctor	Analyses adjusted for child's milk diet (breastfeeding vs bottle), parental history of AD or asthma, maternal

New Zealand Birth cohort of New Zealand N=1141 (data on AD up to 2 years) N=1067	(cereals, vegetables, dairy products, meat, fruits, egg or related products), which the child had been given during the first 4 months. Categorized as follows: 0, 1-3, 4+ food groups	information on doctor-diagnosis of AD, up to 2 and 10 years of age Increased diet diversity within the first 4 months of age: increased risk of AD up to 2 years (1.6 times increased risk: 4+ food groups versus no foods), increased risk of recurrent/chronic AD up to 10 years (2.5 times increased risk: 4+ food groups versus no foods),	education
Nwaru B et al. 2014[120] Finnish Type 1 Diabetes Prediction and Prevention study Prospective Cohort Study Finland Sample Size: Baseline N: 4074 Analytic N: 3781 Attrition: 93% Sex: 1646 boys (52%), 1496 (48%) girls Race/Ethnicity: not mentioned	Intervention/Exposure: The child's diet was assessed by using age-specific dietary questionnaires at ages 3, 4, 6, and 12 months and a follow-up ''age at introduction of new foods'' form for recording the age at introduction of complementary foods. Looked at: the number of complementary foods introduced at 3, 4, 6, and 12 months of age. 4 categories of food diversity at each time point were defined based on the distribution of the data at each time point: at 3 months, these were ''no food item,'' ''1-2 food items,'' and ''>2 food items''; at 4 months, these were ''no food item,'' ''1-2 food items,'' ''3-4 food items,'' and ''>4 food items''; at 6 months, these were ''0-4 food items,'' ''5-6 food items,'' ''7-8 food items,'' and ''>8 food items''';	Asthma, wheeze, atopic eczema, and allergic rhinitis were analysed. AD: parental reports of doctor-diagnosis ever up to 5 years. International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire for assessment of allergy symptoms No association between diet diversity at the age of 3, 4 months and AD up to 5 years. Reduced diet diversity at 6 months: increased risk of AD up to 5 years (OR and 95% CI: 0-4 food items vs > 8 items: 1.39, 0.88-2.19; 5-6 items vs > 8 items: 1.32, 0.96-1.81; 7-8 items vs > 8 items: 1.38, 1.11-1.71)	**Confounders:** Confounders adjusted for: sex of the child, number of siblings, parental asthma, parental rhinitis, delivery hospital, and maternal smoking during pregnancy. **Limitations:** - The study recruited children carrying genetic risk (HLA-conferred susceptibility) for type 1 diabetes. Therefore, may reduce generalizability of findings to general population - The number of statistical tests performed could mean that the type 1 error rate might not be at the 0.05 level. DD definition was not validated and could be improved with increasing the variety

Atopic Disease Risk Status: 16% and 62% of parents had asthma and rhinitis respectively	at 12 months, these were ‘‘0-7 food items,’’ ‘‘8-9 food items,’’ ‘‘10-11 food items,’’ and ‘‘>11 food items Food groups used as DD definition: cow’s milk and formula (as a combined variable); potatoes; carrots; turnip; fruits and berries (as a combined variable); cereals (rye, wheat, oats, and barley as a combined variable); other cereals (maize, rice, millet, and buckwheat as a combined variable), meat; fish; egg; cabbage; spinach; and lettuce. Assessment Methods: Prospective Parent questionnaires Assessment of DD age: birth to 12 months of age		
Roduit C et al. JACI 2012[121] Prospective birth cohort study Protection Against Allergy Study in Rural Environments (PASTURE/EFRAIM). Stratified in farm and non-farm children Sample Size: Baseline N: 1133 Analytic N: 1041	Diversity of diet in 1st year of life: summing the number of different types of solid food, which were introduced within the 1st year of life -> 2 scores were measured: 1. Diversity score (score 0-6) including food items, which were introduced among about 80% of the children, in total 6 groups: vegetables/fruits, cereals, bread, meat, cake and yogurt. Score used as a continuous variable and a categorized variable (0-3, 4-5, 6 food groups) 2. Diversity score (score 0-15), including all food items: any cow’s milk, yogurt, other milk products, eggs, nuts, vegetables or fruits, cereals, bread, meat, fish, soy, margarine, butter, cake, and chocolate.	AD: parental report of doctor-diagnosis up to 4 years and/or positive SCORAD score during medical examination at the age of 1y (total: 27.1% with AD up to 4y). Increased diet diversity within 1st year of life: reduced risk of AD up to 4 years of age (exclusion children with onset within 1st year of life) (for each additional food introduced in 1st year, reduction of 25% of AD) (aOR for each additional food item: 0.75, 95% CI 0.62-0.91)	Outcome assessment mainly based on parental reports of doctor-diagnosis. To take into account reverse causality: analysis with exclusion of children with AD within the 1st year of age

Table 5: The association between diet diversity and asthma/allergic rhinitis

Roduit C et al 2014[16] Protection Against Allergy Study in Rural Environments (PASTURE/EFRAIMP) Prospective Cohort Study Austria, Finalnd, France, Germany, Switzerland Sample Size: Baseline N: 1133 Analytic N: 848 (asthma) 806 (rhinitis) Attrition: 25% asthma 29% rhinitis Sample Size Calculation: NR Sex: 49.5% female Race/Ethnicity: NR Atopic Disease Risk Status: 53.6% parental history of atopy Background Diet: 47.4% non-exclusively breast fed at least 6 months	Intervention/Exposure: See table – Food Allergy.	Asthma/Allergic Rhinitis assessed at 6 years Assessment Methods: Questionnaires were administered in interviews or self-administered to the mothers within the third trimester of pregnancy and when the children were 2,12, 18, and 24 months of age and then yearly up to age 6 years. Findings: *Asthma*: Increased diet diversity in first year of life was associated with linear trend in protection against development of reported asthma, 26% reduction for the introduction of each successive food. *Allergic Rhinitis*: no significant relationship noted between diversity and the development of allegic rhinitis (linear trend p=0.31, p=0.29 for inhalant sensitisation)	Confounders: Confounders adjusted for: Centre, living on a farm, atopic Fhx, breast feeding, gender, siblings, maternal education Limitations: - Use of reported doctor-diagnosis and possible lack of assessment for resolved transient childhood wheezing - Use of asthma medications was not part of the asthma definition - While analysis was adjusted for confounders, were these the optimal ones to choose - Use of 1 month recall period in assessing new food introduction

Table 6: Summary of diet diversity on Allergy Outcomes

Allergy outcome	Increased risk with higher DD	Reduced risk with higher DD	No effect
Sensitization		+ (4.5 yrs) [food] [16] + (6 yrs) [food] [16] + (up to 15 yrs) [aero-allergens] [109] +(yrs 5) [110]	+ (4.5 yrs) [inhalant] [16] + (6 yrs) [inhalant] [16]
Food Allergy		+ (up to 6 yrs) [16]	
Atopic Dermatitis	+(2 yrs) [114] + (6 yrs) [114] + (2 yrs) [116] + (3 yrs)[117] + (10 yrs) [113,118,119]	+ (2 yrs) [111,112] + (1 yr) [120] + (5 yrs) [120] + (4 yrs) [121] +(2 yrs) [115]	+ (4 yrs) [114] + (6 yrs) [111,112]
Asthma/Wheeze		+ (6 yrs) [16] + (5 yrs)[120]	
Rhinitis		+ (5 yrs)[120]	+(6yrs) [16]

Table 7 : Modified Delphi Panel Regarding Diet Diversity Statements

Statement	Agree	Disagree	Percent Agreement between those who voted	Comments
1. Diet diversity scores should be weighted depending on the types of food being measured (e.g. a diverse fast food diet is not equal to a diverse fruit and vegetable diet).	23	1	95.8%	
2. Diversity of intake of specific foods e.g. range of fruits eaten, different types of cheese consumed, different types of home-cooked or processed foods cannot be used to describe diet diversity but the term diversity of fruit intake, diversity of cheese intake, or diversity of processed food intake can be used. These foods can however be included in combination with other foods to determine overall diet diversity.	22	2	91.67%	1. I would suggest separating the first sentence for clarity. Anyhow, I agree with this statement. 2. The diversity of fruits and vegetables is important to quantify and acknowledge in the overall definition of diet diversity, the diversity of types of cheese and other food groups is less so. 3. Need a better explanation.
3. Diversity of intake of foods containing specific nutrients or ingredients e.g. foods containing advanced glycation end products or foods containing omega-3 fatty acids cannot be used to describe diet diversity but the terms diversity of advanced glycation end products intake or diversity of food containing omega-3 fatty acid intake can be used. These foods can however be included in combination with other foods to determine overall diet diversity. Following comments we have changed the wording to: In these instances, diversity may have a positive (fruit and vegetables) or a negative) (advanced glycation end products) connotation. This list may continue to grow as we gain more knowledge about foods/nutrients with immunomodulatory potential e.g. bovine trans fatty acids which are isomers of linoleic acid.		3	87.5%	1. We do not have any data to suggest that diversity of high AGE foods has a positive effect on dietary diversity. 2. There is a need for high level of knowledge and intellectual capacity to appropriately understand and answer this question. I do not think there is many people who can talk about diversity of advanced glycation end products.
4. For allergy (asthma, food allergy, eczema, rhinitis, allergen sensitivity), there is the opportunity to measure food microbial diversity which relates to the microbial content of foods. Following comments we have changed the wording to: There is the opportunity to measure food microbial diversity which relates to the microbial content of foods.	20	3	87%	1. The formulation of the question is unclear as to what is the relation to "For allergy" (to determine the sensitization capacity of the food? To use the food as microbiome-modulating agent? To treat allergy with microbes on the food?) 2. It is unclear what "For allergy" means here. Also, the whole question is unclear. It is technically possible, but not very feasible at the point of care. Is it a general question what we should recommend to pursue more in the future? 3. I would assume that this can be extended to other food related clinical entities, not only allergies
5. For allergy (asthma, food allergy, eczema, rhinitis, allergen sensitivity), there is the opportunity to measure food biodiversity which relates to the taxonomic classification of food intake e.g. classifying tomatoes as Solanum (genus) opposed to vegetables. Following comments we have changed the wording to:: There is the opportunity to measure food biodiversity which relates to the taxonomic classification of food intake e.g. classifying tomatoes as Solanum (genus) opposed to vegetables.	21	1	95.5%	1.This is still a magic area surrounded by echo chambers even among experts. 2. Solanum -- Wow - you picked a good one here. Tomatoes are a fruit, and other members of the genus include potato - vegetable and aubergine - fruit. I believe that in the US data potato (fries) and tomato (sauce) account for about 40% of fruit and vegetable intake in children.

					3. why would this be only true for allergy? what would be the advantage over diversity of vegs? 4. It is unclear what "For allergy" means here. Please see my comment above.
6.	For allergy (asthma, food allergy, eczema, rhinitis, allergen sensitivity), there is the opportunity to measure food allergen diversity which relates to the number and/or amount of food allergens introduced in a given period of time, e.g. the first year of life. It is important to understand that allergic food diversity may not reflect diet diversity as an emphasis on allergic food intake, may lead to an overall reduced diet diversity. Following comments we have changed the wording to: For allergy (asthma, food allergy, eczema, rhinitis, allergen sensitivity), there is the opportunity to measure allergenic food diversity which relates to the number and/or amount of food allergens introduced in a given period of time, e.g. the first year of life. It is important to understand that allergenic food diversity may not reflect diet diversity as an emphasis on allergenic food intake, may lead to an overall reduced diet diversity.	22	0	100%	1. this point is not clear. precisely, food allergen means ara h 1, cor a 9 etc. what you mean is foods which a lot of children are allergic to. there is hardly a food which cannot elicit allergic reactions. 2. Please consider also contact with food allergens other than by the oral route- this can be exposure by inhalation or via skin - so the measurement of allergen intake maybe not sufficient if control of exposure is the question
7.	It is not possible at present to define the minimum amount of allergenic protein that should be consumed in order to be sufficient within the food allergen diversity measure. Following comments we have changed the wording to: It is not possible at present to define the minimum amount of allergenic protein that should be consumed in order to be sufficient within the allergenic food diversity measure. In future, there may be an index that could described the allergenic potential of foods within the context of diet diversity better.	: 21	2	91.3%	Basically agreed, maybe in a short time we will be able to develop a sort of “index” specific by any specific protein, that, in combination with the food allergen diversity measure, could give a more precise idea of the allergenic potential of that protein with in a measure of an allergen diversity patterns. A sort of “diet allergen index” conceptually similar to the glycemic index and again similarly, with two definitions as “allergenic index” and an “allergenic load”. Finally (I have a dream) this could lead to a “personalized allergenic diet” based on the individually defined numbers, on the way of the personalized diet depicted by Elinav and co. at the Welzman one doubts: has someone already described this pathway? Sufficient for allergy prevention? Agree - may be a question of present/absent or the amount and frequency and timing of that. I don't understand "to be sufficient within the food allergen diversity measure"
8.	When possible, studies reporting data of diet diversity should include sensitivity, specificity, true and false positive/negative values to assist future meta-analyses and comparisons but should de-emphasize reporting of a cut-off value for a sample.	20	1	95.2%	1. differentiating between sensitization and allergy would be more helpful 2. Getting this into practice will depend on cut-off values that are clinically meaningful. So, need them. Paper would though present the basic data to allow later meta-analysis. 3. Again, not very clear to me. There are two questions within one sentence. I agree with the first part, 4. but I do not understand clearly the second part. 5. Not sure how this can be done in reality during a study? 6. Sensitivity, specificity, true and false positive/negative

				values are values used for validation studies. it is unclear what their purpose here would be and how they can be derived.
9. For pregnant women we recommend a minimum recall period of 2 week days and 1 weekend day, measured at repeated intervals throughout pregnancy. When possible, portion sizes should be collected and reported.	20	2	90.9%	1. Agree with the need to measure dietary exposure at more than one interval & record portion sizes, but not necessarily the use a recall period of 2 weekdays and 1 weekend day - this rules out the use of FFQs and 24h recalls, which may be more practical methods than a food diary method. 2. Any standard used to define the 2-week period? If mothers can recall up to several months for the child (as question 2 below), then they can also give recall of their own diet over several months. Is there any evidence that 2 weeks is an acceptable period of time?
10. For infants, we recommend food recall periods within the first year of life. These recall periods may include the first four months of life, the first six months of life or the first year of life. Repeated measure of intake is recommended to improve the quality of data, rather than just consuming a particular food/food group once. When possible, portion sizes should be collected and reported. Following comments we have changed the wording to: For infants, we recommend food recall periods within the first year of life. These periods may include the first four months of life, the first six months of life or the first year of life. Repeated measure of intake is recommended to improve the quality of data, rather than just consuming a particular food/food group once. When possible, portion sizes should be collected and reported, and data should be recorded prospectively.	21	2	91.3%	1. "Videotape" techniques should be developed (either at an institution or at home – parents are not reliable. 2. Again, not sure how this can be provided by the participants for practical reasons 3. How far back can parents really remember. Certainly not a year.
11. Investigators should consider ways to ensure measuring how food is prepared/cooked in their study design, and if/when possible, this should be detailed for diet diversity. Ideally foods should be defined as raw, home-cooked, processed or ultra-processed.	22	1	95.7%	1. Methodologies should be carefully defined and agreed, step by step. Caregivers (especially mothers) are extraordinarily able to mix different concentrations all these dines of preparations to get their final purpose.0that infants eat somethings and/or anything whichever the source. 2 What about home-cooked foods that include some processed ingredients e.g. casserole containing canned chickpeas alongside other fresh vegetables. Perhaps a 4th category? 3. Water quality and milk quality are also important points to consider? 4. I agree with the first part of this statement, but not with the need for categorization. These categories are difficult as they are not mutually exclusive, a food could be processed AND home cooked (i.e. canned/frozen vegetables/fruit/fish used in a home cooked recipe). 5. I do not see a big difference between home cooked and processed- since cooking per se is a way of processing foods

12. Age of introduction of solid foods, food allergens and infant formula should be clearly indicated in studies investigating the association between diet diversity and allergy outcomes. Following comments we have changed the wording to: Age of introduction of solid foods, allergenic foods and infant formula should be clearly indicated in studies investigating the association between diet diversity and allergy outcomes	22	0	100%	1. Difficult tasks for the same reasons explained before. Parents should not perceive these surverys as a sort of “drug-us” indication 2. agree but the term "food allergens" should be changed as commented before
13. Introduction of infant formula cannot be classified on its own as diet diversity but should be included in measuring diet diversity of food and food groups. Following comments we have changed the wording to: Introduction of infant formula cannot be classified on its own as diet diversity but should be included in measuring diet diversity of food and food groups. Introduction of infant formula may in fact reduce diet diversity as Breastmilk potentially exposes an infant to the diversity of the maternal diet, whereas formula is uniform.	23	0	100%	1. This is difficult. Perhaps this statement needs a caveat? Using this definition, it would mean that an infant who is formula fed would be classified as having a more diverse diet than an infant who is exclusively breastfed? Breastmilk potentially exposes an infant to the diversity of the maternal diet, whereas formula is uniform.

[a] Threshold for consensus was set at 18 votes in favour of the statement (75% of the 24 panel members).

Box 1: Definitions: Dietary diversity, dietary variety, dietary quality, dietary patterns
Diet: Food intake

Nutritional adequacy: The comparison between the nutrient requirement and nutritional intake of an individual or population.[2]

Dietary diversity: can be defined as the number of different foods or food groups consumed over a given reference period, and it is not a proxy for nutrient adequacy.[1]

Dietary variety: a term often used in the literature, is considered synonymous to dietary diversity.[1]

Dietary quality: no official definition in the literature. Definitions vary widely, and many different measurement tools are used. Diet quality may reflect nutrient adequacy but it is not always the case.[1]

Dietary patterns: reflect an individual's food choice and differ across nationality, culture, socio-economic class and religion. Dietary patterns represent an overall view of food intake may be a better indicator of disease risk than studying specific foods and nutrients.[3]

Complementary food: "When breast milk is no longer enough to meet the nutritional needs of the infant, complementary foods should be added to the diet of the child. The transition from exclusive breastfeeding to family foods, referred to as complementary feeding, typically covers the period from 6 to 18-24 months of age, and is a very vulnerable period"[4]

Sensitisation to food allergens: Sensitisation is defined as the presence of allergen-specific IgE (sIgE)) to food allergens without having clinical symptoms on exposure to those foods,[5]

IgE mediated food allergy: requires both the presence of specific IgE to the food (sensitisation) and the development of signs and symptoms when exposed to the food.[5]

Food Frequency Questionnaire: A questionnaire which enquires about the frequency of consumption of a specific list foods over a period of time[6]
Semi-quantitative/quantitative food frequency questionnaire: ask about portion size, gathered either by using free description, as standardized portions or a choice of portion sizes in addition to frequency of consumption.
Quantitative food frequency questionnaire uses measures of food eaten e.g. measures such as grams or mls as opposed to using measures such as portion sizes/cups/spoons [7]

24 hour recall: gathers information about all foods and drinks (and nutritional supplements in some cases) consumed over the previous 24 hours.[8]

Processed food: considered to be natural foods manufactured with the addition of salt or sugar.[9]