**Dietary Strategies for the Prevention of Asthma in Children**

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**Abstract**

*Purpose of the review*

This review summarizes information relating to dietary intake during pregnancy, lactation and early life that may prevent childhood asthma. This review also summarizes how future studies may be improved.

*Recent findings*

Recent findings from observational studies suggest that eating according to certain dietary patterns during pregnancy, such as the dietary inflammatory index, Mediterranean diet and Maternal diet index, may reduce asthma and or wheeze in the child. Vitamin D supplementation with higher doses than recommended during pregnancy may be associated with reduced early transient childhood wheezing in the offspring. Higher levels of omega-3 fatty acids in breast milk may be protective against childhood asthma. Breastfeeding infants has been shown to offer many benefits to mother and child but a direct relationship between breastfeeding and the development of asthma has not been established. During childhood, infants and children may need to reduce their intake of advanced glycation end products (AGEs), increase their food intake according to the traditional Mediterranean diet and increase the diversity of foods eaten.

*Summary*

Current evidence provides limited suggestions regarding dietary changes for preventing early transient childhood wheezing. In order to harmonize methods for future data collection and reporting, it is important to harmonize relevant definitions and other important factors. The aim of the considerations described here is to enable better comparison of future studies and provide better guidance to patients and families.

*Keywords:* Prevention, Maternal diet, Infant diet, Asthma

**1. Introduction**

Allergic diseases are an increasing public health concern.1,2Asthma, eczema, allergic rhinitis and food allergies form the four major presentations of allergic diseases. Allergic diseases affect more than 50 million Americans.1 Asthma is reported to affect 300 million people world-wide3 and 10.4% of children in the US have a diagnosis of asthma.4 Early life factors, including dietary intake during pregnancy, lactation and early life, have been considered as possible risk factors for the development of childhood asthma. However, despite data from a pool of studies focusing on dietary intake and asthma outcomes, the results do not give clear guidance on which dietary factors to address.5,6 It is also unclear when the intervention should be commenced and discontinued. Results and conclusions for systematic reviews are clearly different when data from pregnancy, breastfeeding and early life feeding practices are treated as distinct entities vs. pooling data from interventions covering more than one time period.5,7 Globally, recommendations on dietary intake during pregnancy, lactation and early life for prevention of asthma are sparse and most guidelines focus on interventions for the prevention of eczema and/or food allergies.8-11 The limited information on dietary interventions to prevent asthma/wheeze is further confirmed by the Global Initiative for Asthma (GINA) guidelines.12 These guidelines suggest that correcting vitamin D deficiency in pregnant women or women who plan to get pregnant may reduce offspring wheeze. Breastfeeding is advised for reasons other than preventing asthma.12 After a review of available guidelines, Linneman et al.13 concluded that there is no need to exclude allergens from the maternal diet for asthma prevention. Further, observational studies in early life suggest that a Mediterranean style diet in younger children is associated with a lower prevalence of asthma.6

Two nutrients have in particular been hypothesized to play a role in the prevention of wheeze and/or asthma and will be highlighted in this review. The active metabolite of vitamin D, 1,25-(OH)2D3, has immunomodulatory activity, and deficiency of this metabolite has been proposed as a factor in the increase of asthma and allergic diseases in the recent decades. Although studies relating to wheeze and asthma outcomes focus on vitamin D intake/supplement, correcting vitamin D levels may also have to correct lifestyle changes. Safe-sensible UVB exposure however, may be the most effective method of ensuring sufficient vitamin D exposure and has been associated with reduced eczema outcomes.14 Current reference ranges for “normal” vitamin D levels, similar to dietary recommendations, mainly reflects ranges for reducing rickets and are not focused on “immunological and nutritional health benefits.

The immunomodulatory effects of omega-3 fatty acids have also been highlighted and described in many studies.15 Nutrients however, do not exist in isolation and to fully understand the role of dietary intake on disease outcomes, it is important to study food and nutrient intake using a whole diet approach. Three terms that are used to describe and summarize overall diet intake are diet patterns, diet indices and diet diversity.6 Diet patterns is a term used to describe food intake, usually in relation to cultural eating practices. Diet indices summarize food intake to describe the quality of the diet. Diet diversity is defined as the number of different foods or food groups consumed over a given reference period. Diet variety,a term often used in the literature, is considered synonymous with diet diversity*.6,16* The mechanistic basis for how overall dietary intake potentially affects allergy outcomes needs further clarification, but may ultimately be mediated through an effect on the microbiome and subsequent immune modulation or a direct effect of increased intake of immunomodulatory nutrients.6,17

Studying asthma as an outcome, is also not without its pitfalls. Early childhood wheeze may not lead to allergic asthma outcomes in later childhood, as not all infants/young children who wheeze will develop asthma.18 Therefore, we will focus on reported asthma/wheeze in children 3 years and older whenever this data is available.

The overall aim of this review is to summarize the role of dietary intake during pregnancy, lactation and early life on the development of childhood asthma while highlighting concerns with research findings and possible solutions (Table 1).

**2. Pregnancy**

**2.1. Observational data**

**2.1.1. Foods and nutrients**

An EAACI systematic review7 reported that intake of vitamin D, Vitamin E, zinc, fruits and vegetables, nuts, fish/fatty fish and meat during pregnancy were associated with reduced offspring asthma or wheeze across all ages. Factors associated with an increased risk of offspring asthma or wheeze were the consumption of pasta, fish sticks and arachidonic acid (ARA) during pregnancy. However, the authors mention that the doses of foods or nutrients studied were heterogeneous and were not consistent with current nutrition guidelines, which make practical implementation of the findings troublesome.

**2.1.2. Food components**

*Advanced glycation end products*

Observational data indicates that increased intake during childhood of foods typical of the Western diet, such as burgers, sugar and high fructose corn syrup,19 and food preparations, such as frying, may be associated with the increase in allergic diseases, particularly asthma.20 These foods are sources of advanced glycation end products (AGEs), compounds which form when sugar binds to protein or it is formed via lipoxidation.19 AGEs may contribute to the development of asthma via their effect on both Th2 and inflammatory cytokines. This is referred to as the false alarm hypothesis.20 Asthma and wheeze are characterized by underlying inflammatory processes. The Receptor for Advanced Glycation End Products (RAGE) is activated by dietary intake of AGEs which leads to up-regulation of TNF-α, IL-1, IL-6 and IL-8.21 RAGE and its activation ligands are central to the development of allergic responses and sensitization seen in asthma.20,22,23 In addition, higher levels of soluble RAGE (a decoy ligand) is protective against asthma.24 Despite this compelling information, Venter et al. did not find any association between maternal AGEs intake during pregnancy and offspring asthma outcomes before or after adjusting for potential confounders.25

**2.1.3.****Food patterns and indices**

Four diet indices in pregnancy have been studied in relation to asthma outcomes; (i) dietary inflammatory index,26-28 (ii) the healthy eating index,26,29,30 (iii) the Mediterranean diet index.29,31-34 and (iv) the Maternal diet index.35 A number of other food patterns have also been studied, primarly indentified from studies using principal component analysis. 36,37

*Dietary inflammatory index*

The dietary inflammatory index (DII) is a complex index that provides an estimate of the inflammatory potential of the diet based on the combination of foods and nutrients with high and low inflammatory potential in single index.38 Positive weights are assigned to inflammatory foods and nutrients, such as trans fats, and negative weights to less or anti-inflammatory nutrients, such as omega-3 fatty acids. One recent study showed an association between maternal energy-adjusted dietary inflammatory index26 scores during pregnancy and offspring asthma outcomes over 10 years. Another study found an association between maternal DII scores27 and offspring wheeze trajectories, but not asthma, up to 7.5 years of age. Venter et al.28 concluded that their results suggested that a maternal diet that scored higher on the DII was associated with increased odds of offspring asthma and/or wheeze by age 4 years.

*Healthy eating index*

Three studies have used the Healthy Eating Index (HEI) as a measure of healthy eating to study the role of dietary intake in pregnancy on childhood allergy outcomes.26,29,30 The Food Allergy and Intolerance Research Study (FAIR), UK, showed that the Alternate Healthy Eating Index in pregnancy (AHEI-P) was not associated with any allergic outcomes (including asthma) in the offspring at 3 or 10 years.30 Lange et al.29 reported data from Project Viva cohort (US) and found no association between the HEI and recurrent wheeze and children at the age of 3 years. In contrast, Chen et al.26 used data from an Irish cohort and reported that higher HEI-2015 scores were associated with lower risk of asthma in the offspring up to 10 years.

*Mediterranean diet index*

Associations between the Mediterranean diet index and asthma/wheeze outcomes have been reported by 5 studies29,31-34 (two from Spain, one from Greece, one from the USA and one from the UK). Reduced outcomes of childhood persistent wheeze, atopic wheeze and atopy was associated with the Mediterranean diet index in only one of the studies.33 Another study34 found a protective association between the Mediterranean diet score and childhood maximal mid-expiratory flow, as well as FEF25-75% z-scores.

*Maternal diet index*

Venter et al.35 developed an index of maternal diet during pregnancy, using data from the Healthy Start study, Colorado (US). The index was associated with reduced odds of any allergy in a birth cohort of >1200 mother-offspring dyads up to 4 years of age. The index was associated with 16% reduced odds of asthma and 20% reduced odds of wheeze in offspring by four years.35

*Other diet patterns or indices*

Using principal component analysis, two studies showed that a maternal Western diet pattern was associated with a reduced risk of wheeze,36,37 which highlights the complexities of studying diet intake during pregnancy and offspring allergy outcomes. The generation R study found no significant association between maternal diet quality in pregnancy and asthma at 10 years. 39

**2.2. Randomized controlled trials**

*Vitamin D*

A systematic review with meta-analysis7 reported that prenatal supplementation with vitamin D in doses higher than recommended by most countries, may have beneficial effects for prevention of asthma/wheeze in the offspring. RCT doses included 800 IU, 2400 IU, and 4000 IU. (<https://www.aafp.org/news/health-of-the-public/20101201iomrpt-vitdcal.html>) The Institute of Medicine recommendations for intake of vitamin D are summarized in Table 2.

*Omega-3 fatty acids*

The same meta-analysis that summarized vitamin D interventions7 also indicated that there was a trend towards a protective effect for omega-3 supplementation during pregnancy, on offspring asthma/wheeze outcomes, but it did not reach statistical significance. The Institute of Medicine recommendations for intake of omega-3 fatty acids are summarized in Table 3.

**3. Breastfeeding**

**3.1. Observational studies**

**3.1.1. Foods and nutrients**

*Omega-3 fatty acids*

High levels of *n*-6 PUFAs in breast milk have been associated with an increased risk for asthma-like symptoms.40 In addition, another study reported reduced offspring asthma in allergic mothers with higher omega-3 levels in breast milk and increased offspring asthma in non-allergic mothers who had higher omega-6 levels in breast milk.41 Contrary to this, Lumia et al.42 reported that maternal fatty acid intake during lactation did not influence offspring risk of asthma by 5 years of age. Huan and Yang43 reported on two studies44,45 showing that omega-3 fatty acid levels in expressed breast milk are inversely associated with offspring asthma when comparing highest to the lowest group of omega-3 fatty acid levels. Studying the role of omega-3 fatty acids in allergy outcomes may need to be extended beyond merely studying supplementation and include monitoring of serum or erythrocyte fatty acid levels. We don’t only need to address omega-3 supplements but also address that ratio of omega 3:omega-6 fatty acids. On a basic immunological level, sufficient omega-3 levels are required for cardiolipin function in mitochondria. In mitochondria with suboptimal levels of cardiolipin, mitrochondria in naïve T cells conserve energy by directing expression of Th2 cells rather than Th1 cells.46,47 To alter 50% of omega-3 on a cardiolipin molecule can take several hundred days, indicating that long-term supplementation may be required to improve clinical outcomes.

**3.1.2.****Food patterns and indices**

There is currently no published data on the association between overall maternal diet during breastfeeding and offspring asthma outcomes.

**3.2. Randomized controlled trials**

*Vitamin D*

In a UK based study, breastfeeding mothers (*n* = 164) of infants with facial eczema at their 1 month check-up were randomly assigned to receive either vitamin D3 supplements (*n* = 82; 800 IU/day) or placebo (*n* = 82) for a six week period. There was no difference in reported wheeze between the groups up to 2 years of age.48

**3.3. Breastfeeding duration**

A recent systematic review by the United Kingdom Food Standards Agency concluded that they did not find any evidence for any duration of breastfeeding on asthma prevention in the offspring.5 This is echoed by the GINA guidelines.12 However, breastfeeding is always recommended for the many other benefits to both mother and infant.49

**4. Early life**

**4.1. Observational studies**

**4.1.1. Nutrients and food**

*Fish intake/omega-3 fatty acids*

Kull et al. reported that regular fish consumption during the first year of life was associated with a reduced risk for allergic disease by age 4.50 A systematic review focusing on fish intake in infancy concluded that fish intake, not specifically, omega-3 fatty acids, during infancy may prevent allergic outcomes, although no association was seen between infant fish intake and childhood asthma outcomes.51

*Vitamin D*

A prospective birth cohort study of 123 infants recorded vitamin D3 intake during the first year of life and dichotomized intake as equal to or less than 13.00 ug per day, or higher than 13.00 ug/day. By 6 years of age, allergic manifestations including asthma were more prevalent in the group with higher intake of vitamin D3.52 In support of this, Kull et al. reported that children supplemented with vitamins A and D in water-soluble form, as opposed to those children that received their supplements in a fat soluble form, during the first year of life had an almost 2-fold increased risk of asthma by 4 years of age.53

**4.1.2. Food components**

*Advanced glycation end products*

A study from the US indicated that increased AGEs intake in children 5-9 years of age was significantly associated with increased odds of wheezing, wheeze-disrupted sleep, and wheezing requiring prescription medication.54

**4.1.3.****Food patterns, indices and diversity**

*Diet indices*

In children, studies focusing on the Mediterranean diet report on *current* dietary intake for asthma outcomes, and therefore do not assess the preventative efffect of early (infancy) dietary intake with later (childhood) asthma outcomes. Three systematic reviews focusing on dietary intake and asthma outcomes concluded that the Mediterranean diet (using the Mediterranean diet index) in childhood55-57 shows an inverse relationship with reported wheeze and asthma. Papamichael et al.56 reported an inverse association between Mediterranean diet pattern and asthma in children. Nurmatov et al.55 and Lv et al. 57 reported a possible association between the Mediterranean diet and reduced prevalence of childhood wheeze.

*Other dietary patterns*

A number of studies showed an increased prevalence of wheeze/asthma in children consuming a Western diet.58-60 In contrast to these studies, the Dutch Generation R cohort did not find an association between a healthy dietary pattern in early life and a lower risk of atopic diseases, including asthma, in childhood.39,61

*Diet diversity*

Data relating to diet diversity in infancy and asthma/wheeze in childhood were reported by the PASTURE study62 and the Finnish Type I Diabetes Prediction and Prevention Study Prospective Cohort Study.63 In the PASTURE cohort, Roduit et al.62 showed that increasing diet diversity in the first year of life was associated with reduced asthma by 6 years. In fact, a 26% reduction was reported for each additional food introduced. Nwaru et al.63 noted that reduced diet diversity at 12 months of life was associated with a greater risk for the development of asthma at age 5, as well as an increased risk for any wheeze.

**4.2. Randomized controlled trials**

*Omega-3 and omega-6*

Four papers reported using omega-3 and omega-6 supplementation in newborns with a family history of allergy for the first 6 months of life.64-67 The active arm contained 135mg DHA & 32 mg EPA. No differences in the prevalence of asthma or wheeze were seen between the two arms when children were 5 years of age. The outcomes wheeze ever, doctor visits for wheeze, bronchodilator use and nocturnal coughing at 18 months were significantly reduced in children in the higher exposure quintiles to omega-3 fatty acids. Reduced prevalence of any wheeze and a reduction in prevalence of wheeze for more than one week by 18 months was reported for the group receiving omega-3 supplements. Birch et al.68 supplemented healthy term infants with docosahexanoic acid (DHA; 0.32%-0.36% of total fatty acids) and ARA (0.64%-0.72% of total fatty acids) vs. a placebo for the first year of life. Infants fed formula supplemented with DHA and ARA had a reduced incidence and delayed onset of upper respiratory infection and wheezing/asthma by 3 years of age. D'Vaz et al. 69 supplemented infants at high risk of allergy for the first 6 months with eicosapentanoic acid (EPA) and DHA (280 mg DHA & 110 mg EPA) vs. placebo for the first 6 months of life. Elevated plasma levels of DHA and total omega-3 fatty acid levels at 6 months of age were associated with a reduced risk of recurrent wheeze in the first 12 months of life. Foiles et al.70 supplemented healthy term infants with DHA and ARA (0.64% of total fatty acids as ARA and either 0.32, 0.64 or 0.96% of total fatty acids as DHA) vs. a placebo throughout infancy. The risk of skin and respiratory allergic diseases in childhood was influenced by a maternal history of allergies. Incidence of wheezing/asthma were significantly lower in the subgroup who received the fatty acid supplement and whose mothers reported a positive history of allergy compared to those with no supplementation and a maternal history of allergy. Fatty acid supplementation did not show any effect on allergy outcomes compared to no supplementation in children with no maternal history of allergy.

*Vitamin D*

Children of mothers with 25-hydroxyvitamin D levels ≥50 nmol/L were randomized to receive oral vitamin D supplementation of 400 IU/day (*n* = 97) or a placebo (*n* = 98) for the first six months of life. There was no significant difference for reported wheeze by 1 year of age or for wheeze/asthma at 2.5 years between the two groups.71 This may once again highlight the importance of sun exposure rather than supplementation. Studies focusing on vitamin D intake may also show improved outcomes by adding a vitamin K2 supplement to increase vitamin D receptors.72

**5. Conclusion**

Overall, the data suggests that eating according to certain dietary patterns during pregnancy such as the DII, Mediterranean diet and Maternal diet index may reduce asthma and/or wheeze in the child. Vitamin D supplementation in pregnancy may be associated with reduced asthma outcomes in the offspring. No conclusion can be drawn regarding the effect of maternal diet during lactation but higher levels of omega-3 fatty acids in breast milk may be protective. Infants should ideally be breastfed for the many benefits to mother and child. Limited data suggest that infants and children may want to reduce their intake of AGEs, increase food intake according to the Mediterranean diet and to increase the diversity of foods eaten. In order to harmonize methods for future data collection and reporting, it is important to harmonize relevant definitions and other important factors such as timing of supplementation, nutrient interactions and environmental exposures e.g. sunlight. It is hoped that the considerations described here will enable better comparison of future studies to provide improved guidance to patients and families.

**Key points (figure 1):**

A) During pregnancy, eating a less inflammatory diet, and eating according to the Mediterranean diet and according to the Maternal diet index may reduce asthma and/or wheeze in the child.

B) No conclusion can be drawn regarding the effect of maternal diet during lactation, but higher levels of omega-3 fatty acids in breast milk may be protective.

C) Reducing intake of AGEs, increasing food intake aligning with the traditional Mediterranean diet and methods (mainly plant based, slow cooked meats with herbs), and increasing the diversity of foods eaten during infancy and early childhood may prevent the development of asthma in later childhood.

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**References**

1. Food Allergies: Global Burden, Causes, Treatment, Prevention and Public Policy. National Academy of Sciences, 2017. (Accessed September 2021) <http://www.nationalacademies.org/hmd/Activities/Nutrition/FoodAllergies.aspx>.)

2. Global atlas of Allergy. 2014.(Accessed September 2021) <http://www.eaaci.org/globalatlas/GlobalAtlasAllergy.pdf>.)

3. The WAO White Book on Allergy (Update. 2013). 2013. (Accessed September 2021) <https://www.worldallergy.org/UserFiles/file/WhiteBook2-2013-v8.pdf>.)

4. Mirabelli MC, Hsu J, Gower WA. Comorbidities of asthma in U.S. children. Respir Med 2016;116:34-40.

5. Garcia-Larsen V, Ierodiakonou D, Jarrold K, et al. Diet during pregnancy and infancy and risk of allergic or autoimmune disease: A systematic review and meta-analysis. PLoS Med 2018;15:e1002507.

6. Venter C, Greenhawt M, Meyer RW, et al. EAACI position paper on diet diversity in pregnancy, infancy and childhood: Novel concepts and implications for studies in allergy and asthma. Allergy 2020;75:497-523.

7. \*Venter C, Agostoni C, Arshad SH, et al. Dietary factors during pregnancy and atopic outcomes in childhood: A systematic review from the European Academy of Allergy and Clinical Immunology. Pediatr Allergy Immunol 2020;31:889-912.

*This is the systematic review underpinning the EAACI prevention guidelines. The paper concludes:*

*1) Prenatal supplementation with vitamin D may prevent offspring.*

*2) No consistent patterns for other nutrients and foods were found for asthma and allergy prevention.*

*3) Studies using similar methodology and outcome measures are required.*

8. Netting MJ, Campbell DE, Koplin JJ, et al. An Australian Consensus on Infant Feeding Guidelines to Prevent Food Allergy: Outcomes From the Australian Infant Feeding Summit. J Allergy Clin Immunol Pract 2017;5(6):1617-1624

9. Turner PJ, Feeney M, Meyer R, Perkin MR, Fox AT. Implementing primary prevention of food allergy in infants: New BSACI guidance published. Clin Exp Allergy 2018;48:912-5.

10. \*Halken S, Muraro A, de Silva D, et al. EAACI guideline: preventing the development of food allergy in infants and young children (2020 update). Pediatr Allergy Immunol 2021; 32(5):843-858.

*This is the latest summmary guidelines on food allergy prevention from EAACI.*

*The paper concludes that:*

*1) There is uncertainty on how to prevent food allergy*

*2) Introduction of well-cooked egg and peanut in the first year of life may prevent egg and peanut allergy*

*3) Supplementation with cow’s milk formula in the first week of life should be avoided*

11. \*\*Fleischer DM, Chan ES, Venter C, et al. A Consensus Approach to the Primary Prevention of Food Allergy Through Nutrition: Guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology. J Allergy Clin Immunol Pract 2021; 9(1):22-43.

*This is the latest consensus document from North America and Canada on food allergy prevention.*

*The paper concludes that:*

*1) Peanut and egg should be introduced around 6 months of life, but not before 4 months for prevention of peanut and egg allergy.*

*2) Other allergens should be introduced once solid food introduction commences.*

*3) Maternal avoidance of food allergens during pregnancy and/or lactation to prevent food allergy is not recommended.*

12. \*Global initiative for asthma. Global strategy for asthma management and prevention - 2021 update. 2021 (Accessed September 2021) https://ginasthma.org/gina-reports/

*This is the latest guidance from GINA.*

*The guidelines conclude that:*

*1) There is limited information on dietary interventions to prevent asthma/wheeze*

*2) The guidelines suggest that correcting vitamin D deficiency in pregnant women or women who plan to get pregnant may reduce offspring wheeze.*

*3) Breastfeeding is advised for reasons other than preventing asthma.*

13. Larenas Linnemann DES, Del Río Navarro BE, Luna Pech JA, et al. Recommendations for the prevention and diagnosis of asthma in children: Evidence from international guidelines adapted for Mexico. Allergol Immunopathol (Madr) 2018;46:291-303.

14. Rueter K, Jones AP, Siafarikas A, Chivers P, Prescott SL, Palmer DJ. The Influence of Sunlight Exposure and Sun Protecting Behaviours on Allergic Outcomes in Early Childhood. Int J Environ Res Public Health 2021;18(10), 5402.

*This paper describes the likely importance in sunexposure in allergy prevention*.

15. \*\*Venter C, Eyerich S, Sarin T, Klatt KC. Nutrition and the Immune System: A Complicated Tango. Nutrients 2020;  20;12(11):3554.

*This review summarizes the complexity of factors between diet and allergy or asthma prevention.*

*The paper concludes that:*

*1) There is enthusiasm for the potential of diet to impact the immune system and prevent disease*

*2) Nutrition scientists is challenged by defining and conducting nutrition research*

*3) Further studies of dietary patterns, immune system and gut microbiome composition and function, and subsequent epigenetic modifications are needed to improve current knowledge of diet-immune system interactions.*

16. Ruel MT. IS DIETARY DIVERSITY AN INDICATOR OF FOOD SECURITY OR DIETARY QUALITY? A REVIEW OF MEASUREMENT ISSUES AND RESEARCH NEEDS. International Food Policy Research Institute 2002:1-58. (Accessed September 2021) https://www.ifpri.org/publication/dietary-diversity-indicator-food-security-or-dietary-quality

17. Laursen MF, Andersen LB, Michaelsen KF, et al. Infant Gut Microbiota Development Is Driven by Transition to Family Foods Independent of Maternal Obesity. mSphere 2016;1(1):e00069-15.

18. Biagini Myers JM, Schauberger E, He H, et al. A Pediatric Asthma Risk Score to better predict asthma development in young children. J Allergy Clin Immunol 2019;143:1803-10.e2.

19. Uribarri J, Woodruff S, Goodman S, et al. Advanced glycation end products in foods and a practical guide to their reduction in the diet. J Am Diet Assoc 2010;110:911-16 e12.

20. Smith PK, Masilamani, M., Li, X., Sampson, H.A. “The False Alarm” hypothesis: Food allergy is associated with high dietary advanced glycation end products and pro-glycating dietary sugars that mimic alarmins. Journal of Allergy and Clinical Immunology 2017l 139(2):429-437.

21. Guarneri F, Custurone P, Papaianni V, Gangemi S. Involvement of RAGE and Oxidative Stress in Inflammatory and Infectious Skin Diseases. Antioxidants (Basel) 2021;10 (1):82.

22. Hammad H, Lambrecht BN. Barrier Epithelial Cells and the Control of Type 2 Immunity. Immunity 2015;43:29-40.

23. Ullah MA, Loh Z, Gan WJ, et al. Receptor for advanced glycation end products and its ligand high-mobility group box-1 mediate allergic airway sensitization and airway inflammation. J Allergy Clin Immunol 2014;134:440-50.

24. Lyu Y, Zhao H, Ye Y, et al. Decreased soluble RAGE in neutrophilic asthma is correlated with disease severity and RAGE G82S variants. Mol Med Rep 2018;17:4131-7.

25. \*\*Venter C, Pickett K, Starling A, et al. Advanced glycation end product intake during pregnancy and offspring allergy outcomes: A Prospective cohort study. Clin Exp Allergy 2021; doi: 10.1111/cea.14027.

*This is the first paper with extensive data on maternal intake of AGEs during pregnancy.*

*1) The data shows no effect on chilhood asthma and allergy outcomes.*

*2) Exposure to AGes during pregnancy may not have the same impact on child allergy and asthma outcomes as postnatal exposure.*

26. Chen LW, Lyons B, Navarro P, et al. Maternal dietary inflammatory potential and quality are associated with offspring asthma risk over 10-year follow-up: the Lifeways Cross-Generation Cohort Study. Am J Clin Nutr 2020;111:440-7.

27. Hanson C, Rifas-Shiman SL, Shivappa N, et al. Associations of Prenatal Dietary Inflammatory Potential with Childhood Respiratory Outcomes in Project Viva. J Allergy Clin Immunol Pract 2020; 8(3):945-952

28. \*\*Venter C, Palumbo MP, Sauder KA, et al. Examining Associations Between Dietary Inflammatory Index in Pregnancy, Pro-inflammatory Cytokine and Chemokine Levels at Birth, and Offspring Asthma and/or Wheeze by Age 4 Years. J Acad Nutr Diet 2021; 121(10):2003-2012.

*This is paper investigates the role of a pro-inflammatory diet during pregnancy on chilhood asthma outcomes.*

*The authors found:*

*1) limited statistical significant associations between a pro-inflammatory diet in pregnancy and offspring asthma/wheeze outcomes*

*2) no statistical significant associations between a pro-inflammatory diet in pregnancy and cord blood cytokines and chemokines*

*3) no statistical significant associations between cord blood cytokines and chemokines and childhood asthma/wheeze outcomes*

29. Lange NE, Rifas-Shiman SL, Camargo CA, Jr., Gold DR, Gillman MW, Litonjua AA. Maternal dietary pattern during pregnancy is not associated with recurrent wheeze in children. J Allergy Clin Immunol 2010;126:250-5, 5 e1-4.

30. Moonesinghe H, Patil VK, Dean T, et al. Association between healthy eating in pregnancy and allergic status of the offspring in childhood. Ann Allergy Asthma Immunol 2016;116:163-5.

31. Castro-Rodriguez JA, Ramirez-Hernandez M, Padilla O, Pacheco-Gonzalez RM, Perez-Fernandez V, Garcia-Marcos L. Effect of foods and Mediterranean diet during pregnancy and first years of life on wheezing, rhinitis and dermatitis in preschoolers. Allergologia et Immunopathologia 2016;44:400-9.

32. Chatzi L, Garcia R, Roumeliotaki T, et al. Mediterranean diet adherence during pregnancy and risk of wheeze and eczema in the first year of life: INMA (Spain) and RHEA (Greece) mother-child cohort studies. Br J Nutr 2013;110:2058-68.

33. Chatzi L, Torrent M, Romieu I, et al. Mediterranean diet in pregnancy is protective for wheeze and atopy in childhood. Thorax 2008;63:507-13.

34. Bedard A, Northstone K, Henderson AJ, Shaheen SO. Mediterranean diet during pregnancy and childhood respiratory and atopic outcomes: birth cohort study. Eur Respir J 2020;55.

35. \*Venter C, Palumbo MP, Glueck DH, et al. The Maternal Diet Index in Pregnancy is associated with offspring allergic diseases: The Healthy Start Study. Allergy 2021; doi: 10.1111/all.14949

*The first paper that reports on an overall healthy diet index and offspring allergy outcomes.*

*The authors reported 1) childhood asthma outcomes 2) allergic rhinitis 3) and atopic dermititis when pregnant women consumed a diet with a higher maternal diet index (i.e. healthier diet consisting of more vegetebles and yogurt and less fried, fatty, sugary and low fiber foods).*

36. Loo EXL, Ong L, Goh A, et al. Effect of Maternal Dietary Patterns during Pregnancy on Self-Reported Allergic Diseases in the First 3 Years of Life: Results from the GUSTO Study. International Archives of Allergy & Immunology 2017;173:105-13.

37. Miyake Y, Okubo H, Sasaki S, Tanaka K, Hirota Y. Maternal dietary patterns during pregnancy and risk of wheeze and eczema in Japanese infants aged 16-24 months: the Osaka Maternal and Child Health Study. Pediatr Allergy Immunol 2011;22:734-41.

38. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hebert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr 2014;17:1689-96.

39. Nguyen AN, Elbert NJ, Pasmans S, et al. Diet Quality throughout Early Life in Relation to Allergic Sensitization and Atopic Diseases in Childhood. Nutrients 2017;9:05.

40. Notenboom ML, Mommers M, Jansen EH, Penders J, Thijs C. Maternal fatty acid status in pregnancy and childhood atopic manifestations: KOALA Birth Cohort Study. Clinical & Experimental Allergy 2011;41:407-16.

41. van Elten TM, van Rossem L, Wijga AH, et al. Breast milk fatty acid composition has a long-term effect on the risk of asthma, eczema, and sensitization. Allergy 2015;70:1468-76.

42. Lumia M, Luukkainen P, Tapanainen H, et al. Dietary fatty acid composition during pregnancy and the risk of asthma in the offspring. Pediatr Allergy Immunol 2011;22:827-35.

43. Yang H, Xun P, He K. Fish and Fish Oil Intake in Relation to Risk of Asthma: A Systematic Review and Meta-Analysis. PLOS ONE 2013;8:e80048.

44. Wijga AH, van Houwelingen AC, Kerkhof M, et al. Breast milk fatty acids and allergic disease in preschool children: the Prevention and Incidence of Asthma and Mite Allergy birth cohort study. J Allergy Clin Immunol 2006;117:440-7.

45. Lowe AJ, Thien FC, Stoney RM, et al. Associations between fatty acids in colostrum and breast milk and risk of allergic disease. Clin Exp Allergy 2008;38:1745-51.

46. Herbst EA, Paglialunga S, Gerling C, et al. Omega-3 supplementation alters mitochondrial membrane composition and respiration kinetics in human skeletal muscle. J Physiol 2014;592:1341-52.

47. Faas MM, de Vos P. Mitochondrial function in immune cells in health and disease. Biochim Biophys Acta Mol Basis Dis 2020;1866:165845.

48. Norizoe C, Akiyama N, Segawa T, et al. Increased food allergy and vitamin D: randomized, double-blind, placebo-controlled trial. Pediatr Int 2014;56:6-12.

49. James DC, Dobson B. Position of the American Dietetic Association: Promoting and supporting breastfeeding. J Am Diet Assoc 2005;105:810-8.

50. Kull I, Bergstrom A, Lilja G, Pershagen G, Wickman M. Fish consumption during the first year of life and development of allergic diseases during childhood. Allergy 2006;61:1009-15.

51. Zhang GQ, Liu B, Li J, et al. Fish intake during pregnancy or infancy and allergic outcomes in children: A systematic review and meta-analysis. Pediatr Allergy Immunol 2017;28:152-61.

52. Back O, Blomquist HK, Hernell O, Stenberg B. Does vitamin D intake during infancy promote the development of atopic allergy? Acta Dermato-Venereologica 2009;89:28-32.

53. Kull I, Bergström A, Melén E, et al. Early-life supplementation of vitamins A and D, in water-soluble form or in peanut oil, and allergic diseases during childhood. J Allergy Clin Immunol 2006;118:1299-304.

54. \*\*Wang JG, Liu B, Kroll F, et al. Increased advanced glycation end product and meat consumption is associated with childhood wheeze: analysis of the National Health and Nutrition *Examination Survey. Thorax 2021;76:292-4.*

 *Paper highlights association between childhood AGEs intake and asthma outcomes.*

*The authors reported that higher AGE intake was significantly associated with increased 1) childhood wheeze, 2) wheeze-disrupted sleep and 3) wheezing requiring medical treatment in children age 5 – 13 years.*

55. Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. J Allergy Clin Immunol 2011;127:724-33 e1-30.

56. Papamichael MM, Itsiopoulos C, Susanto NH, Erbas B. Does adherence to the Mediterranean dietary pattern reduce asthma symptoms in children? A systematic review of observational studies. Public Health Nutr 2017;20:2722-34.

57. Lv N, Xiao L, Ma J. Dietary pattern and asthma: a systematic review and meta-analysis. Journal of asthma and allergy 2014;7:105-21.

58. de Cassia Ribeiro Silva R, Assis AM, Cruz AA, et al. Dietary Patterns and Wheezing in the Midst of Nutritional Transition: A Study in Brazil. Pediatr Allergy Immunol Pulmonol 2013;26:18-24.

59. Lee SC, Yang YH, Chuang SY, Liu SC, Yang HC, Pan WH. Risk of asthma associated with energy-dense but nutrient-poor dietary pattern in Taiwanese children. Asia Pac J Clin Nutr 2012;21:73-81.

60. Ellwood P, Asher MI, Garcia-Marcos L, et al. Do fast foods cause asthma, rhinoconjunctivitis and eczema? Global findings from the International Study of Asthma and Allergies in Childhood (ISAAC) phase three. Thorax 2013;68:351-60.

61. Tromp, II, Kiefte-de Jong JC, de Vries JH, et al. Dietary patterns and respiratory symptoms in pre-school children: the Generation R Study. Eur Respir J 2012;40:681-9.

62. Roduit C, Frei R, Depner M, et al. Increased food diversity in the first year of life is inversely associated with allergic diseases. J Allergy Clin Immunol 2014;133:1056-64.

63. Nwaru BI, Takkinen HM, Kaila M, et al. Food diversity in infancy and the risk of childhood asthma and allergies. J Allergy Clin Immunol 2014;133:1084-91.

64. Marks GB, Mihrshahi S, Kemp AS, et al. Prevention of asthma during the first 5 years of life: a randomized controlled trial. J Allergy Clin Immunol 2006;118:53-61.

65. Peat JK, Mihrshahi S, Kemp AS, et al. Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. J Allergy Clin Immunol 2004;114:807-13.

66. Mihrshahi S, Peat JK, Webb K, et al. Effect of omega-3 fatty acid concentrations in plasma on symptoms of asthma at 18 months of age. Pediatr Allergy Immunol 2004;15:517-22.

67. Mihrshahi S, Peat JK, Marks GB, et al. Eighteen-month outcomes of house dust mite avoidance and dietary fatty acid modification in the Childhood Asthma Prevention Study (CAPS). J Allergy Clin Immunol 2003;111:162-8.

68. Birch EE, Khoury JC, Berseth CL, et al. The impact of early nutrition on incidence of allergic manifestations and common respiratory illnesses in children. J Pediatr 2010;156:902-6, 6 e1.

69. D'Vaz N, Meldrum SJ, Dunstan JA, et al. Postnatal fish oil supplementation in high-risk infants to prevent allergy: randomized controlled trial. Pediatrics 2012;130:674-82.

70. Foiles AM, Kerling EH, Wick JA, Scalabrin DM, Colombo J, Carlson SE. Formula with long-chain polyunsaturated fatty acids reduces incidence of allergy in early childhood. Pediatric Allergy & Immunology 2016;27:156-61.

71. \*Rueter K, Jones AP, Siafarikas A, Lim EM, Prescott SL, Palmer DJ. In "High-Risk" Infants with Sufficient Vitamin D Status at Birth, Infant Vitamin D Supplementation Had No *Effect on Allergy Outcomes: A Randomized Controlled Trial. Nutrients 2020;12 (6):1747.*

*Paper highlights that:*

*1) Vitamin D supplementation in infants who showed sufficient levels of vitamin D at birth did not affect immune cell development during the first 6 months of life.*

*2) Immune indices at birth and at 6 months of age were associated with early life atopic dermatitis.*

72. Dahlquist DT, Dieter BP, Koehle MS. Plausible ergogenic effects of vitamin D on athletic performance and recovery. J Int Soc Sports Nutr 2015;12:33.

**Table 1: Difficulties with determining study outcomes and future recommendations**

Legend:

Current problems with presented research finding and suggestions or recommendations on improving future studies

**Table 2: Institute of Medicine recommendations for vitamin D intake**

Legend:

Institute of Medicine recommendations for the intake of vitamin D throughout the lifespan.

**Table 3: Institute of Medicine recommendations for omega-3 fatty acid intake**

Legend: Institute of Medicine recommendations for the intake of omega-3 fatty acids throughout the lifespan.

**Figure 1: Summary of current data regarding** **Dietary Strategies for the Prevention of Asthma in Children**

Legend: Dietary factors associated with reduced asthma/wheeze in childhood:

Pregnancy: Reduced scores on the Diet inflammatory index, Increased scores on the

Mediterranean diet index and Vitamin D supplementation

Breastfeeding: Increased Omega-3 fatty acid levels in breast milk

Infancy: Reduced intake of advanced glycation end products , Omega-3 fatty acid supplementation