



Review

Does maternal diet during pregnancy and lactation affect outcomes in offspring? A systematic review of food-based approaches



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ABSTRACT

Objectives: The aim of this study was to investigate the relationship between maternal diet during pregnancy and lactation and development of atopic disorders in childhood.

Methods: We included studies published up to August 2011 that assessed food-based maternal dietary interventions or that examined associations between maternal dietary intake during pregnancy and/or lactation and allergic outcomes (eczema, asthma, hay fever, and sensitization) in their children.

Results: We included 42 studies (>40 000 children): 11 intervention studies (including 7 randomized control trials), 26 prospective cohort studies, 4 retrospective cohort studies, and 1 case-control study. In the randomized control trials, no significant difference was noted overall in the prevalence of eczema and asthma in the offspring of women on diets free from common food allergens during pregnancy. The prospective cohorts investigated a large number of potential associations, but reported few significant associations between maternal dietary intake and development of allergy. Maternal diets rich in fruits and vegetables, fish, and foods containing vitamin D and Mediterranean dietary patterns were among the few consistent associations with lower risk for allergic disease in their children. Foods associated with higher risk included vegetable oils and margarine, nuts, and fast food.

Conclusion: This review did not find widespread or consistent links between mothers' dietary intake and atopic outcomes in their children. However, maternal consumption of Mediterranean dietary patterns, diets rich in fruits and vegetables, fish, and vitamin D-containing foods were suggestive of benefit, requiring further evaluation.

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Introduction

The prevalence of allergic diseases in most industrialized countries has increased over the past 20 y and is now estimated to affect one in five individuals [1–3]. Common manifestations of allergic disease include allergic rhinitis or hay fever, asthma, eczema or atopic dermatitis, and food allergies. The risk for allergic disease is increased to about one in three if one first-degree relative (parent or sibling) is atopic and to 70% if both

parents are atopic [4]. The pattern of allergy expression differs with age; with the greatest incidence of food allergy and atopic eczema peaking by 1 y of age, whereas asthma and allergic rhinitis continue to increase until around 15 y of age [5]. Many childhood allergies persist, with about 50% of childhood asthma sufferers and 80% of hay fever sufferers continuing to have symptoms into adulthood [6,7]. The cost to the health care system and the burden for the family are high [8,9] and it is estimated that asthma alone costs in excess of \$34 billion annually [10].

The increase in allergic disease has occurred too rapidly (within one to two generations) to be a result of population genetic changes, so it is likely related to environmental changes.

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Throughout the industrialized world, strong evidence exists that environmental factors accompanying higher socioeconomic conditions and hygiene standards have contributed to the increased prevalence of allergic disease. Societies with fewer respiratory infections, greater use of antibiotics early in life, fewer older siblings in the household, less contact with farm animals, and general lack of early microbial exposure are repeatedly associated with the greatest burden of allergic disease [11]. The atopic predisposition is believed to arise where the infant has an innate tendency to produce immunoglobulin (Ig)E antibodies (sensitization), which in some individuals progresses to allergic disease. The allergens causing sensitization are nearly always proteins originating from the environment including pollens, house dust mite, or food. Why children are becoming increasingly sensitized to environmental allergens is a matter of debate. Several factors may be involved, including whether the child is breastfed from birth [12], the child's antioxidant status [13], the balance of ω -6 to ω -3 polyunsaturated fatty acids in the diet [14] and environmental influences such as microbial exposure, cigarette smoke, and other pollutants [15].

Because many infants develop allergic symptoms early in infancy, and exposure to allergens may be important in the development of food allergies, there is great interest in maternal dietary strategies during pregnancy and lactation that may prevent childhood allergies, and thus reduce the burden of disease. This systematic review evaluates the effect of food-based approaches in the maternal diet for the prevention of childhood allergies.

Methods

Inclusion criteria

We included studies of any design that either compared a food-based maternal dietary intervention during pregnancy and/or lactation with another intervention or no intervention. We also included studies that examined associations between maternal dietary intake during pregnancy and/or lactation and allergic outcomes in their children from that pregnancy (cohort and case–control studies). Studies with cointerventions, such as timing of introduction of solid foods into the child's diet, use of hydrolyzed formula and non-food-based interventions such as dust mite control were eligible for inclusion.

We prespecified primary outcomes as child eczema, asthma, hay fever, and food allergy and secondary outcomes as allergy symptoms, atopy or atopic disorder, dyspnea, hay fever (allergic rhinitis or allergic rhinoconjunctivitis), wheeze (and recurrent wheeze), cough, food hypersensitivity (IgE-mediated food allergy or food intolerance), and sensitization (e.g., milk, egg, nut, food, inhalant).

We excluded studies assessing infantile colic, as this was not considered an allergic outcome.

As maternal intake needed to be food based, intervention studies designed to assess the effect of dietary supplements were not eligible for inclusion, nor were those where dietary intakes were expressed only in terms of nutrients.

We excluded studies that only investigated maternal nut (including peanut) consumption during pregnancy and/or lactation because nut allergy (particularly peanut) warrants a separate examination and assessment.

Searching

We searched MEDLINE, EMBASE, and the Cochrane Library (last searched end of August 2011) and scanned reference lists of systematic reviews and other relevant retrieved papers for additional studies.

Search terms included prenatal, antenatal, maternal, mother, pregnan*, lactat*, breastf*, intake, consumption, food, diet, wheez*, dermatitis, eczema, atop*, asthma, allerg*, food allergy hypersensitivity. The full search strategy is documented in the appendix.

Study selection and data extraction

Two authors independently assessed search results against study eligibility criteria. Two authors also independently conducted data extraction for each included study.

Data synthesis

Where possible, the results of randomized controlled trials (RCTs) were pooled, using the meta-analysis program RevMan [16]. We used risk ratios with 95% confidence intervals to express dichotomous outcomes. Where statistical heterogeneity was substantial ($I^2 > 40\%$), we used a random-effects model. Differences between subgroups were assessed using interaction tests [17].

The results of non-randomized intervention studies were narratively reported.

The results from cohort and case–control studies were tabulated and narratively summarized. Where available, we reported the adjusted outcomes for these study designs. Results were presented by age of children, with the youngest age first.

Risk for bias

For RCTs, we assessed the risk for bias using the methods outlined in the Cochrane Handbook for Reviews of Interventions [17]. For other study designs we took account of the risk for selection bias, attrition bias, and reporting bias.

Results

This systematic review included 42 studies. Table 1 lists the characteristics of the included studies. Eleven studies were intervention (7 RCTs, 1 participant preference trial, and 3 non-randomized comparisons). These studies examined the effect of eliminating or restricting common allergens from the maternal diet during pregnancy and lactation. Some included cointerventions such as manipulation of the infant's diet, or environmental measures.

The remaining 31 studies were 26 prospective cohorts, 4 retrospective cohorts, and 1 case–control study. These studies looked at the association of different dietary patterns or the frequency of consumption of different foods with atopic outcomes.

One intervention trial and seven other studies were excluded [18–25]. The intervention study reported the outcomes of an intervention based on a supplement rather than food; seven cohort studies reported dietary intakes in terms of nutrients rather than foods.

Results are reported by the major clinical outcomes (eczema, asthma and wheeze, hay fever, sensitization, and food allergy) and study design (intervention or observational).

Risk for bias assessment summary

The risk for bias assessments are described in Table 1 (association studies [26–76]) and in Table 2 (intervention studies [26,29,32,34,36,39,41,42,44,45,78]). Overall, the 11 intervention studies had at least moderate risk for bias. None of the RCTs fully described the methods used to conceal allocations at the time of randomization. Only one study was able to devise a way to blind the intervention and most studies had moderate losses of participants.

The 31 association studies were of reasonable quality: 12 had low risk for bias; 2 had low to moderate risk, and 17 had moderate risk for bias.

Maternal diet and eczema in children

Intervention studies. Five RCTs and two non-randomized comparisons assessed the effects of maternal dietary restriction on eczema in their children (Table 1). The five RCTs examined the effect of avoiding one of more common allergens in the maternal diet during pregnancy and lactation. In a study that randomized 212 women to a diet free of cow's milk and egg during pregnancy and lactation or a normal diet, the development of eczema,

allergic rhinoconjunctivitis, asthma, and food allergy in the offspring up to 5 y of age was tracked [27]. In another study the intervention group was restricted from cow's milk, egg, and peanut consumption and had limited intake of soy and wheat during pregnancy and lactation [34]. Children were followed until 7 y of age and reported any atopic disorder (asthma, food allergy, allergic rhinitis, eczema, and aeroallergen sensitization). In the Isle of Wight Study [36], the 58 women in the intervention group followed a diet that restricted cow's milk, egg, nut, and fish during lactation. This study delayed introduction of allergenic foods in the offspring, and introduced house dust mite control. In one study, women were [39] randomized to a diet without cow's milk during pregnancy and lactation, and in another [32] women followed a diet with a strictly reduced cow's milk and egg intake during late pregnancy. Both trials followed the offspring until 18 mo of age. The first trial reported the development of eczema, and the second reported cord blood IgE, eczema, and asthma. In a non-randomized comparison, [29,30] the children of 65 women who adhered to a diet free of cow's milk, egg, and fish while breast-feeding were compared with the children of 50 women who maintained a normal diet. Solid foods were delayed and the children were followed for eczema and food allergy until 10 y of age. A previous study [41] enrolled 150 pregnant women into a patient preference trial of avoiding cow's milk and egg during pregnancy and lactation. The children were followed until 1 y of age for eczema and sensitization.

In the five RCTs [27,32,34,36,39], there was no significant difference overall in the prevalence of childhood eczema (risk ratio [RR], 0.76; 95% confidence interval [CI], 0.50–1.16; $N = 682$ children, random effects). These trials showed statistical ($I^2 = 44\%$) and clinical heterogeneity with different dietary restrictions and eczema assessed at different ages. The only RCT showing a significant reduction in childhood eczema included house dust mite control as well as dietary restrictions [36]. Due to the heterogeneity, a pooled result for the five RCTs was not presented (Fig. 1).

Two non-randomized comparative studies also showed no evidence for an effect of dietary restriction. In one non-randomized preference trial, 30 women chose to completely avoid milk and eggs in the last trimester of pregnancy and while breastfeeding exclusively; 33 women also avoided all milk and eggs, but only while breastfeeding; and 41 women chose no dietary restrictions [41]. In this study, six children of mothers in each of the avoidance groups had eczema in the first year of life compared with five children in the group where mothers did not follow dietary restrictions.

In a non-randomized concurrent comparison, when mothers followed a diet free from eggs, cow's milk, or fish in the first 3 mo of their baby's life, the infants were significantly less likely to develop eczema up to 6 mo compared with children of mothers who had no dietary restrictions. This effect was not sustained after 6 mo of age or at follow-up when the children were 10 y old [29,30].

Observational studies. Sixteen prospective cohort studies reported eczema in children as an outcome (Table 1). All used adjusted analyses, unless otherwise stated. A detailed summary of each study may be found in Supplementary Table 1.

3 mo to 1 y. Four prospective cohort studies examined the relationship between maternal diet and eczema in children up to 1 y of age. Physician-diagnosed eczema in 3- to 4-mo-old Japanese children was not associated with their mothers' intake of dairy products, eggs, or fish during pregnancy. However, in this population, a significantly increased risk for eczema was noted

with higher levels of meat consumption (>64 g/d) [71]. In two studies, for children up to 1 y of age, daily consumption of about 30 g of fish by their mothers during pregnancy [72] and increased consumption (daily versus less frequently) [53] showed protective effects against eczema. However, neither of these studies adjusted their results for potential confounders. In another unadjusted study [47], increased vitamin C concentration in atopic mothers' breast milk (attributed to dietary intake of vitamin C from fruit and vegetables during lactation) was associated with significantly reduced rates of eczema in their children.

It has been shown that daily maternal fish consumption of about 30 g weakened the otherwise borderline deleterious association between high maternal exposure to pollutants (fine particulate matter measured by environmental air monitors worn by the women and exposure to environmental tobacco smoke) and infant eczema [72].

2 to <3 y. Six prospective cohort studies and one retrospective cohort study examined the relationship between maternal diet and eczema in children from 2 to <3 y of age. Four of the six prospective studies included the same cohort of women and their children, with each study reporting on different maternal dietary exposures.

Two studies compared maternal dietary patterns (healthy, Western, traditional, or processed) [62,75] and two compared consumption of total and individual dairy products [54,68] with childhood eczema at 2 to 3 y of age, and found no significant association. This was also the case for maternal intake of fruit and vegetables in both studies, except that green and yellow vegetables and citrus fruit showed protective associations against eczema in one study [69]. It has previously been noted that there were no significant associations among spinach, celery, cabbage, salad, and citrus fruits [54]. High maternal consumption of margarine and vegetable oils is significantly associated with an increased risk for eczema, but there were no significant associations with eggs, butter, seeds, deep-frying vegetable fat, and nuts [54].

High maternal fish intake (once or twice a week during pregnancy) was associated with significantly lower rates of children's eczema in one study [54]. Another retrospective study with unadjusted analyses [67] failed to find an association between maternal consumption of fish at least once a week during pregnancy and childhood eczema, as found elsewhere [61], where mothers in the highest quartile consumed >70 g of fish a day.

One study [61] failed to find an association between maternal meat intake during pregnancy and childhood eczema.

3 y. Four maternal dietary patterns during pregnancy—a Mediterranean diet, a “healthy” diet, a “prudent” diet and a Western dietary pattern—have been compared [66]. None of these dietary patterns consumed by mothers while pregnant showed significant associations with development of eczema in their children at 3 y of age.

5 y. At least one serving of fish a week by mothers during pregnancy was protective for eczema in their children at 5 y of age in one study, whereas none of the other foods tested (including fruit and vegetables, grains, and fats) showed any consistent associations [58]. One study [60] was unable to find an association between vitamin D from food consumed during pregnancy and development of eczema in children at 5 y of age.

Children's polychlorinated biphenyl (PCB) and mercury levels were measured as markers of maternal dietary intake of fish likely to be contaminated with marine pollutants, and the

Table 1
Characteristics of included studies

Author, Country/Study name	Design	Risk of bias	Number randomized (intervention, control) N (I, C)	Family history of atopy	Type of food intervention (intervention studies) or type of food exposures assessed (cohort studies) Avoidance unless otherwise stated	Timing of intervention or exposure assessment*	Outcomes	Age of child at assessment
Intervention studies								
Falth-Magnusson 1987 [26], 1987 [27], 1992 [28]	RCT	Moderate	212 (104, 108)	Yes	Cow's milk, egg	Pregnancy Lactation	Eczema Allergic rhinoconjunctivitis, asthma, food allergy	≤5 y
Hattevig 1989 [29] 1999 [30] Sweden	Non-randomized comparison	Moderate	115 (65, 50)	Yes	Cow's milk, egg, fish	Lactation Solid foods	Eczema Food allergy	3, 6, 9, 12, & 18 mo; 10 y
Lilja 1989 [31], 1989 [32], 1991 [33]	RCT	Moderate	166 infants (81, 85)	Yes	Cow's milk, egg (allowed traces of cow's milk in margarine and egg wash on breads)	Pregnancy	Cord blood IgE, eczema, asthma	1 y and 18 mo
Zeiger 1989 [34] 1995 [35]	RCT	Moderate	379 recruited (only 288 (103;185) able to be assessed at 4 mo)	Yes	Cow's milk, egg, peanut, limited soy and wheat	Pregnancy Lactation	Any atopic disorder, asthma, food allergy, allergic rhinitis, sensitization (aeroallergens)	4 mo; 1, 2, 4, & 7 y
Arshad 1992 [36]; Hide 1994 [77]; Hide 1996 [37]; Arshad 2007 [38] Isle of Wight study	RCT	Moderate	136 (69, 67)	Yes	Cow's milk, egg, nuts, fish NB: Also dust mite control	Lactation Solid foods	Asthma, eczema, food allergy, Sensitization (aeroallergens and food)	2, 4, & 8 y
Lovegrove 1994 [39] 1996 [40]	RCT	High	26 (12, 14)	Yes Non atopics as control	Cow's milk (dairy food restriction)	Pregnancy Lactation	eczema	6, 12, & 18 mo
Herrmann 1996 [41] Germany	Patient preference trial	High	150 recruited (I: 30: 33: 34 C: 41 able to be assessed)	Yes	Cow's milk, egg	Pregnancy Lactation	Eczema, sensitization (food)	6 & 12 mo
Appelt 2004 [42]	RCT	Unclear	497 (251: 246)	Yes	Cow's milk egg, nuts, fish	Pregnancy Lactation	Sensitization (food)	1, 2, & 7 y
Author, country / Study name	Design	Risk of bias	N	Family history of atopy*	Type of food intervention (intervention studies) or type of food exposures assessed (cohort studies) Avoidance unless otherwise stated	Timing of intervention or exposure assessment*	Outcomes	Age of child at assessment
Intervention studies: eczema management								
Cant 1986 [43]	RCT Crossover intervention	Moderate	19 mother/infant pairs	Yes	Cows milk, egg, chocolate, wheat, nuts, fish, beef, chicken, citrus fruits, colorings, preservatives	Lactation	Eczema	6 wk to 6 mo
Palmer 2008 [44] Australia	Prospective cohort then randomized, blinded maternal food challenge	Low	32 mother/infant pairs (14:16)	Yes	Egg	Lactation	Eczema	0–6mo
Uenishi 2011 [45] Japan	Prospective cohort, then maternal food exclusion challenge	High	92 mother/infant pairs	Yes	Tree-nut related foods (chocolate, coffee), fermented foods (cheese, yogurt, soy sauce, miso soup, fermented soy)	Lactation	Eczema	< 1 y
Cohort or Case Control Studies								
INTAKE UNLESS OTHERWISE STATED								
Vance 2004 [46]	Prospective cohort	Moderate (some losses to follow-up)	229 mother/infant pairs	Yes	Egg	Pregnancy Lactation	Atopy	6, 12, & 18mo
Hoppu 2005 [47] Finland	Prospective cohort	Moderate (details only presented for univariate analyses)	34 mother/infant pairs	Yes	Fruit and vegetables	Lactation	Eczema, sensitization (food, aeroallergens)	1 y

Salam 2005 [48]	Nested case–control study	Low–moderate (recall bias likely)	691 (279:412)	Mixed	Fish	Pregnancy	Asthma	≥10y
Calvani 2006 [49] Italy APAL study	Retrospective cohort	Moderate (partial adjustment only; recall bias likely)	988 mother/infant pairs	295 atopic 693 non-atopic mothers	Butter Margarine Fish	Pregnancy	Sensitization (food, aeroallergens)	5 y
Camargo 2007 [50] USA (Project Viva)	Prospective cohort	Low (adjusted, low losses to follow-up)	1194 mother/infant pairs	Mixed	Cows milk	Pregnancy	Wheeze	3 y
Devereux 2007 [51] Scotland	Prospective cohort	Moderate (some losses to follow-up)	1924 mother/infant pairs	Mixed	Vitamin D from food	Pregnancy	Wheeze	5 y
Fitzsimon 2007 [52] Ireland	Prospective cohort	Moderate (some losses to follow-up)	631 mother/infant pairs	Unknown	Fruit and vegetables	Pregnancy	Asthma	3 y
Romieu 2007 [53] Spain	Prospective cohort	Low (adjusted, low losses to follow-up)	458 mother/infant pairs	Mixed	Fish	Pregnancy	Ecema sensitization (aeroallergens)	1 y 4 y
Sausenthaler 2007 [54] Germany (LISA)	Prospective cohort	Low (adjusted, low losses to follow-up)	2641 mother/infant pairs	Mixed	Cow's milk products, eggs, fats and oils, seeds, vegetables, fruit, nuts	Pregnancy	Ecema, sensitization (food, aeroallergens)	1 y 2 y
Willers 2007 [55] Scotland	Prospective cohort	Low (adjusted, low losses to follow-up)	1253 mother/infant pairs	Mixed	Fish, fruit, vegetables, grains, fats	Pregnancy	Ecema, asthma, wheeze, rhinitis	5 y
Chatzi 2008 [56] Menorca	Prospective cohort	Low (adjusted, low losses to follow-up)	482 mother/infant pairs	Mixed	Cow's milk products, cereal, nuts, meat	Pregnancy	Wheeze, sensitization (aeroallergens)	6 y
De Batlle 2008 [57] Mexico	Retrospective	Moderate (recall bias likely)	1476 mother/infant pairs	Mixed	Mediterranean diet score	Pregnancy	Asthma, wheeze, rhinitis	6–7 y
Willers 2008 [58] Netherlands (PIAMA)	Prospective cohort	Low (adjusted, low losses to follow-up)	2832 mother/infant pairs	Mixed	Vegetables, fruit fish, egg, cow's milk and milk products, nuts and nut products	Pregnancy	Asthma, wheeze	8 y
Erkkola 2005 [59] Finland	Prospective cohort	Low (low losses but some baseline differences)	1669 mother/infant pairs	Mixed	Cow's milk	Pregnancy Lactation	IgA, IgG levels	1 y
Erkkola 2009 [60] Finland (DIPP Study)	Prospective cohort	Moderate (some losses to follow-up)	1669 mother/infant pairs	Mixed	Vitamin D from food	Pregnancy	Ecema, asthma, allergic rhinitis	5 y
Miyake 2009 [61] Japan (OMCHS)	Prospective cohort	Moderate (some losses to follow-up)	763 mother/infant pairs	Mixed	Fish, meat	Pregnancy	Ecema, wheeze	1 y
Shaheen 2009 [62] UK (ALSPAC)	Prospective cohort	Moderate (some losses to follow-up)	9516 mother/infant pairs	Mixed	Dietary patterns	Pregnancy	Ecema, wheeze, asthma	2 y 7 y
Venter 2009 [63] UK	Prospective cohort	Moderate-High (Moderate losses to follow-up, not clear if adjusted)	969 mother/infant pairs	Mixed	Cow's milk, wheat, fish, peanut	Pregnancy Lactation	Food hypersensitivity	1 y 3 y
Castro-Rodriguez 2010 [64] Spain (EISL)	Retrospective cohort	Moderate (recall bias possible, missing data and some data discrepancies)	1409 mother/infant pairs	Mixed	Dietary patterns Fruit, vegetables, cereal, legumes fats and oils, fish, meat, nuts, eggs, milk, alcohol	Pregnancy	Wheeze	<1 y
Grandjean 2010 [65] Denmark (Faroe Islands)	Prospective cohort	Low (adjusted, low losses to follow-up)	564 mother/infant pairs	Unknown	Fish	Pregnancy	Ecema	5 y 7 y
Lange 2010 [66] US (Project Viva)	Prospective cohort	Low (adjusted, low losses to follow-up)	1376 mother/infant pairs	Mixed	Dietary patterns	Pregnancy	Ecema, asthma, wheeze	3 y
Oien 2010 [67] Norway (PACT)	Retrospective (during pregnancy) cohort	Moderate (recall bias possible, unadjusted)	3086 mother/infant pairs	Unknown	Fish, vegetables	Pregnancy	Ecema, asthma	1 y 2 y
Miyake 2010 [68] Japan (OMCHS)	Prospective cohort	Moderate (high losses to follow-up)	763 mother/infant pairs	Mixed	Cow's milk products	Pregnancy	Ecema, wheeze	1 y
Miyake 2010 [69] Japan (OMCHS)	Prospective cohort	Moderate (high losses to follow-up)	763 mother/infant pairs	Mixed	Vegetables, fruit	Pregnancy	Ecema	1 y
Nwaru 2010 [70] Finland DIPP	Prospective cohort	Low (adjusted, low losses to follow-up)	931 mother/infant pairs	Mixed	Cereals, fruits, vegetables	Pregnancy Lactation	Sensitization (food, aeroallergens)	5 y
Saito 2010 [71] Japan (OMCHS)	Prospective cohort	Moderate (high losses to follow-up)	771 mother/infant pairs	Mixed	Cow's milk, eggs, fish, meat	Pregnancy	Ecema	3–4 mo

(Continued on next page)

Table 1 (Continued)

Author, Country/Study name	Design	Risk of bias	Number randomized (intervention, control) N (I, C)	Family history of atopy	Type of food intervention (intervention studies) or type of food exposures assessed (cohort studies) Avoidance unless otherwise stated	Timing of intervention or exposure assessment*	Outcomes	Age of child at assessment
Jedrychowski 2011 [72] US/Poland	Prospective cohort	Low -Moderate (losses not stated, smokers excluded)	469 mother/infant pairs	Mixed	Fish	Pregnancy	Eczema	1 y
Lumia 2011 [73] Finland DIPP cohort	Prospective cohort	Low (adjusted, low losses to follow-up)	2680 mother/infant pairs	Mixed	Fats, fish, red meat, cow's milk and milk products	Pregnancy	Asthma	5 y
Miyake 2011 [74] Japan (OMCHS)	Prospective cohort	Moderate (high losses to follow-up)	582 mother/infant pairs	Mixed	fish (mercury)	Pregnancy	Eczema, wheeze	3 y
Miyake 2011 [75] Japan (OMCHS)	Prospective cohort	Moderate (high losses to follow-up)	763 mother/infant pairs	Mixed	Dietary patterns	Pregnancy	Eczema, wheeze	1 y
Nwaru 2011 [76] Finland DIPP Nutrition Study	Prospective cohort	Low (but not clear how much maternal diet data was missing)	652 mother/infant pairs	Mixed	General diet Fats and oils, dairy foods, vegetables, eggs, fish, cereals	Lactation	Sensitization (food, aeroallergens)	5 y

ALSPAC, Avon Longitudinal Study of Parents and Children; APAL, The Lazio Association of Pediatric Allergology; DIPP, Diabetes Prediction and Prevention; EISL, International Study of Wheezing in Infants; LISA, Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood; OMCHS, Osaka Maternal and Child Health Study; PACT, Prevention of Allergy among Children in Trondheim; PIAMA, Prevention and Incidence of Asthma and Mite Allergy; RCT, randomized control trial

* Family history of atopy: Yes/No/Mixed (not selected for atopy, but parents asked about this, and results adjusted accordingly)/Unknown

incidence of atopic eczema in the offspring were compared [65]. At 5 y of age, the children with atopic eczema had lower prenatal PCB levels, indicating lower maternal fish intake, compared with those children without eczema.

7 y. No significant associations were found between childhood eczema at 7 y of age and maternal dietary patterns during pregnancy [62].

Lower prenatal PCB levels were reported in children with atopic eczema than in those without eczema, at 7 y of age, as also reported at 5 y of age [65].

Intervention studies related to management of childhood eczema. Three studies [43–45] considered manipulating the maternal diet to manage existing eczema in breastfed children, as opposed to the effects of the maternal diet on preventing eczema.

A crossover RCT [43] studied the effects of maternal exclusion of cow's milk, egg, chocolate, wheat, nuts, fish, beef, chicken, citrus fruits, artificial food colorings, and preservatives during lactation compared with periods of inclusion of cow's milk and eggs on eczema scores in children with eczema ages 6 wk to 6 mo. At each time point, there were no significant differences in eczema scores.

Eczema and sensitization to egg (on skin-prick testing) was studied in 32 exclusively breastfed babies [44]. All mothers had an egg-free diet, followed by a randomized double-blind crossover challenge with egg. An improvement was seen in the eczema score (Scoring Atopic Dermatitis) with time for both the intervention and control groups, but no statistical difference between the groups related to the egg challenge.

The effect of a non-randomized elimination diet and rechallenge with 92 exclusively breastfed children with eczema has been described [45]. Maternal exclusion of chocolate, coffee, and fermented foods (cheese, yogurt, soy sauce, miso soup, and fermented soy beans) for 8 wk during lactation was associated with improved eczema scores in their babies in 67 of 92 cases. Reintroduction of the foods, predominantly chocolate, yogurt, soy sauce, and miso soup into the maternal diet was associated with deterioration in the eczema score.

Maternal diet and asthma or wheeze in children

Intervention studies. Four RCTs [27,32,34,36] assessed the effects of maternal dietary restriction on asthma in children (Table 1). As described previously, one intervention required avoiding cow's milk and egg during pregnancy [32] and two trials continued this restriction while the mother was breastfeeding [27,34]. One study also restricted peanut and limited soy and wheat intake during pregnancy and lactation. In another study [36], the intervention was initiated postpartum, and in addition to avoiding cow's milk, egg, nuts, and fish, also included household dust mite control measures. Pooling of the four RCTs found no significant differences between maternal restricted and unrestricted diets (RR, 0.95; 95% CI, 0.70–1.30; N = 619 children) on development of asthma in children (Fig. 2).

No RCTs reported wheeze as an outcome.

Observational studies. Eighteen prospective cohort studies reported wheeze or asthma in children as an outcome. All used adjusted analyses, unless otherwise stated. Detailed reports of the study results are available in Supplementary Table 2.

Up to 2 y. A retrospective study with unadjusted analyses [67] failed to find an association between maternal consumption of fish at least once a week during pregnancy and childhood asthma.

Table 2

Risk for bias for intervention studies (N = 11)

	Overall risk for bias	Details
Cant 1986 [78]	Moderate	Randomization not reported, not blinded, moderate losses to follow-up
Falsh-Magnusson 1987 [26]	Moderate	Randomization not reported, not blinded, moderate losses to follow-up
Hattevig 1989 [29]	High	Not randomized (matched), not blinded, some non-adherence (crossover)
Lilja 1989 [32]	Moderate	Randomization details not reported, not blinded, low losses to follow-up
Zeiger 1989 [34]	Moderate	Randomization details not reported, not blinded, moderate losses to follow-up
Arshad 1992 [36]	Moderate	Randomization unclear, not blinded, moderate losses to follow-up
Lovegrove 1994 [39]	Moderate	Randomization details not reported, not blinded, moderate losses to follow-up
Hermann 1996 [41]	High	Not randomized (patient preference), not blinded, moderate losses to follow-up
Appelt 2004 [42]	Unclear	No reporting about Randomization, blinding or losses to follow-up (abstract only)
Palmer 2008 [44]	Low	Randomization details not reported, blinded, low losses to follow-up
Uenishi 2011 [45]	High	Not randomized (women acted as own controls), not blinded, high losses to follow-up (most women refused to rechallenged)

Another study [64] reported that antenatal use of olive oil was significantly inversely associated with wheezing in the first year of a child's life.

An inverse relationship was found between a maternal Western dietary pattern and childhood wheeze at 16 to 24 mo, which was no longer apparent when adjusted for maternal α -linolenic acid and vitamin E intake during pregnancy [75]. Neither of the other two dietary patterns in this study (healthy and Japanese) showed any significant associations with childhood wheeze at 16 to 24 mo.

Mercury content of maternal hair samples was measured as an indirect estimate of fish intake during pregnancy; however, no significant difference was found between lower and higher mercury content and childhood wheeze at 29 to 33 mo [74].

3 y. In a retrospective cohort [52], no significant associations were demonstrated between asthma in 3-y-old children and an extensive range of fruits and vegetables eaten by their mothers during pregnancy.

A study involving 3-y-old children [66] failed to find any significant associations between the dietary pattern consumed by the mothers during pregnancy (Mediterranean, Alternate Healthy Eating Index modified for pregnancy, Western, or prudent pattern) and the development of asthma in the children. However, this study found fewer cases of recurrent wheeze in 3-y-old children of women who had a higher Mediterranean diet score compared with those with lower scores. No significant difference in numbers of children with recurrent wheeze at 3 y was observed between the highest and the lowest Alternate Healthy Eating Index modified for pregnancy quartile.

In a U.K. cohort study [62], wheeze in children at 3.5 y (and at 6 mo) was not generally associated with various dietary patterns such as health conscious, traditional, processed, vegetarian, or confectionery.

A moderate to high intake of vitamin D fortified cow's milk during pregnancy has been associated with a lower incidence of wheeze [50].

5 y. No significant associations were noted between consumption of milk and milk products, oils, margarines, butter, other fats, fish, and meat consumed by mothers during pregnancy and occurrence of asthma in their 5-y-old children [73].

No consistent associations was demonstrated between mothers' intake of total fruit, citrus, kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products, or butter versus margarine/low fat spread use during pregnancy and the incidence of asthma in 5-y-old children [58]. However, it was reported that high maternal consumption of apples (>4/wk) appeared to have a protective effect for asthma in children, when assessed as physician-diagnosed

asthma or "ever-had" asthma (but not if assessed as asthma and wheeze in the past 12 mo).

In a nested case-control study [48], high maternal intake of oily fish during pregnancy was found to be protective against early persistent asthma in 5-y-old children, but results for any asthma, early transient asthma, or late-onset asthma were not significant. The protective association of oily fish consumption seemed to be more effective when mothers themselves already had asthma compared with those without asthma. In contrast, this study found maternal consumption (at least monthly during pregnancy) of fish fingers (which contained trans fats) was significantly associated with an increased risk for any asthma in the children.

At 6 to 8 y of age. No significant associations were reported between mothers' dietary patterns while pregnant and development of asthma in their children at 7.5 y of age [62]. A retrospective study [57] also failed to show differences for wheeze in the children.

No association was found between the cereal content of mothers' diets and persistent or atopic wheeze in their 6.5 year old children [56].

When maternal diet during pregnancy was reviewed no significant associations were reported between the frequency of consumption of many foods (vegetables, fish, nuts, egg, milk, or milk products) and any wheeze from 1 to 8 y of age in the children [58]. Only daily, versus rare, maternal consumption of nut products such as peanut butter was associated with an increased risk for wheeze in the children.

Children with asthma at 7 y of age had slightly higher PCB exposures than non-allergic children, although this could be attributed to chance. There was no association with mercury levels [65].

Maternal diet and hay fever or rhinitis in children

Intervention studies. Two studies [34,35] examined maternal elimination of allergens from the diet and included allergic rhinitis or hay fever as outcomes.

The studies reported the results of maternal avoidance of cow's milk, egg, and peanuts during the last trimester of pregnancy and breastfeeding, with delayed and staged introduction of solid foods, compared with standard dietary advice during pregnancy and solids introduced from 4 to 6 mo of age. There were no significant differences in the rates of allergic rhinitis between dietary avoidance and control groups at 4, 12, and 24 mo of age; this was maintained at follow-up at 4 and 7 y of age.

Likewise, another study [28] reported the 5-y follow-up of a cohort of 212 children in which 104 mothers (randomized) eliminated cow's milk and egg from their diet from 28 wk

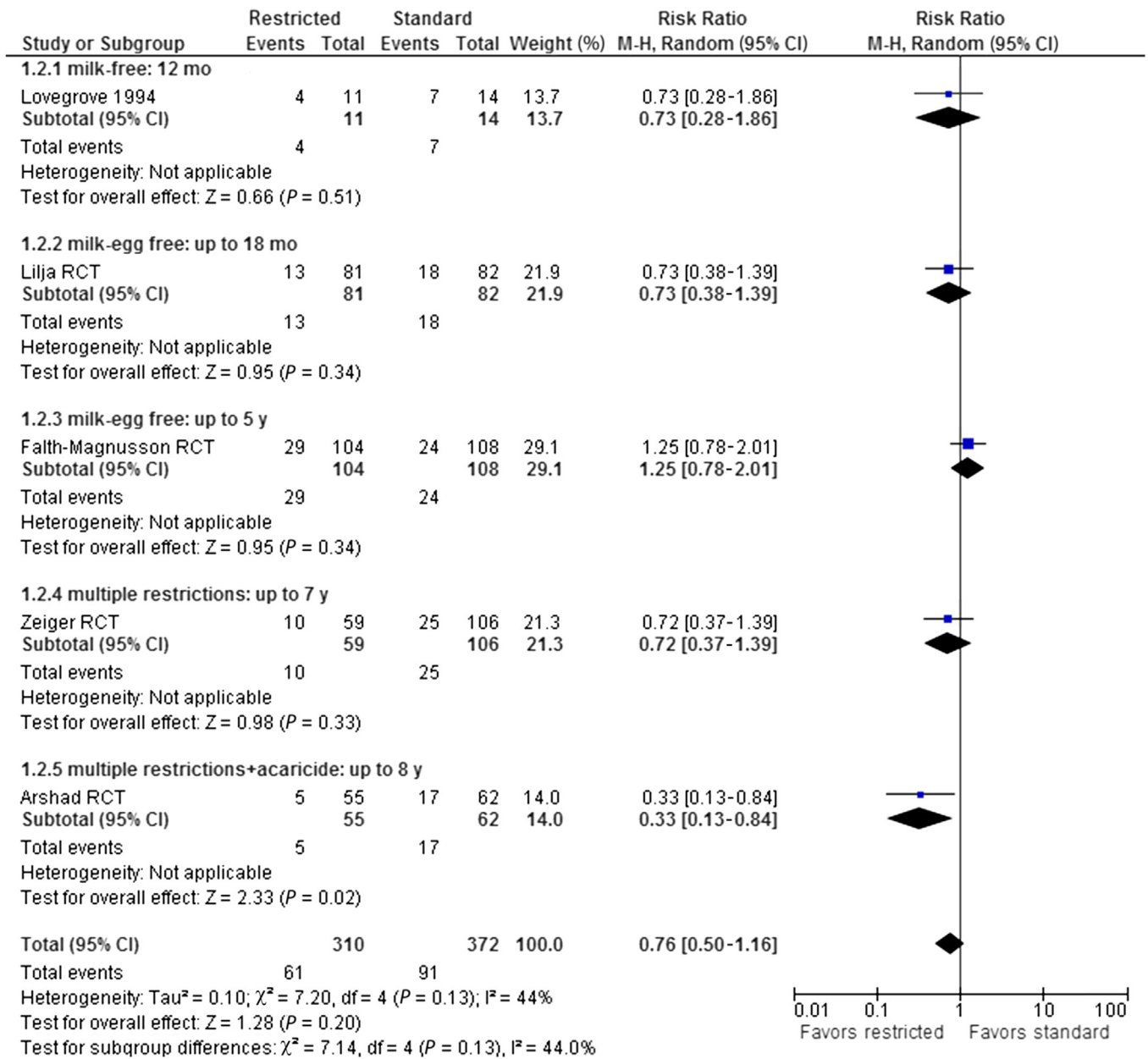


Fig. 1. Forest plot representing the meta-analysis of randomized controlled trials (RCTs) assessing the effect of maternal dietary restriction on childhood eczema.

gestation to birth (and partially during early lactation) versus 108 (randomized) to follow their usual diet (typically 0.5 L milk/d and 3–5 eggs/wk). The elimination group had extra calcium and casein hydrolysate provided. The incidence of allergic rhinitis did not differ between groups.

No meta-analysis was performed as the studies were unsuitable for pooling.

Observational studies. Four cohort studies [50,57,58,62] examined dietary associations that included allergic rhinitis in their outcomes. All studies were prospective cohorts with adjusted analyses, unless otherwise stated.

Dietary associations: diet types. One study [57] compared Mediterranean diet scores for mothers during pregnancy and

reported more sneezing at 6 to 7 y of age in offspring of mothers with lower Mediterranean diet scores.

Another study [62] also assessed the intake of processed foods (meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, and baked beans) in the maternal diet during pregnancy and described more hay fever at 7.5 y of age in children whose mothers had a more highly processed diet, although the difference was lost when the results were adjusted for confounding factors.

Dietary associations: multiple food groups or multiple individual foods

At 5 to 7 y

Vitamin D from food in the maternal diet during the eighth month of pregnancy was looked at [60]. The lowest

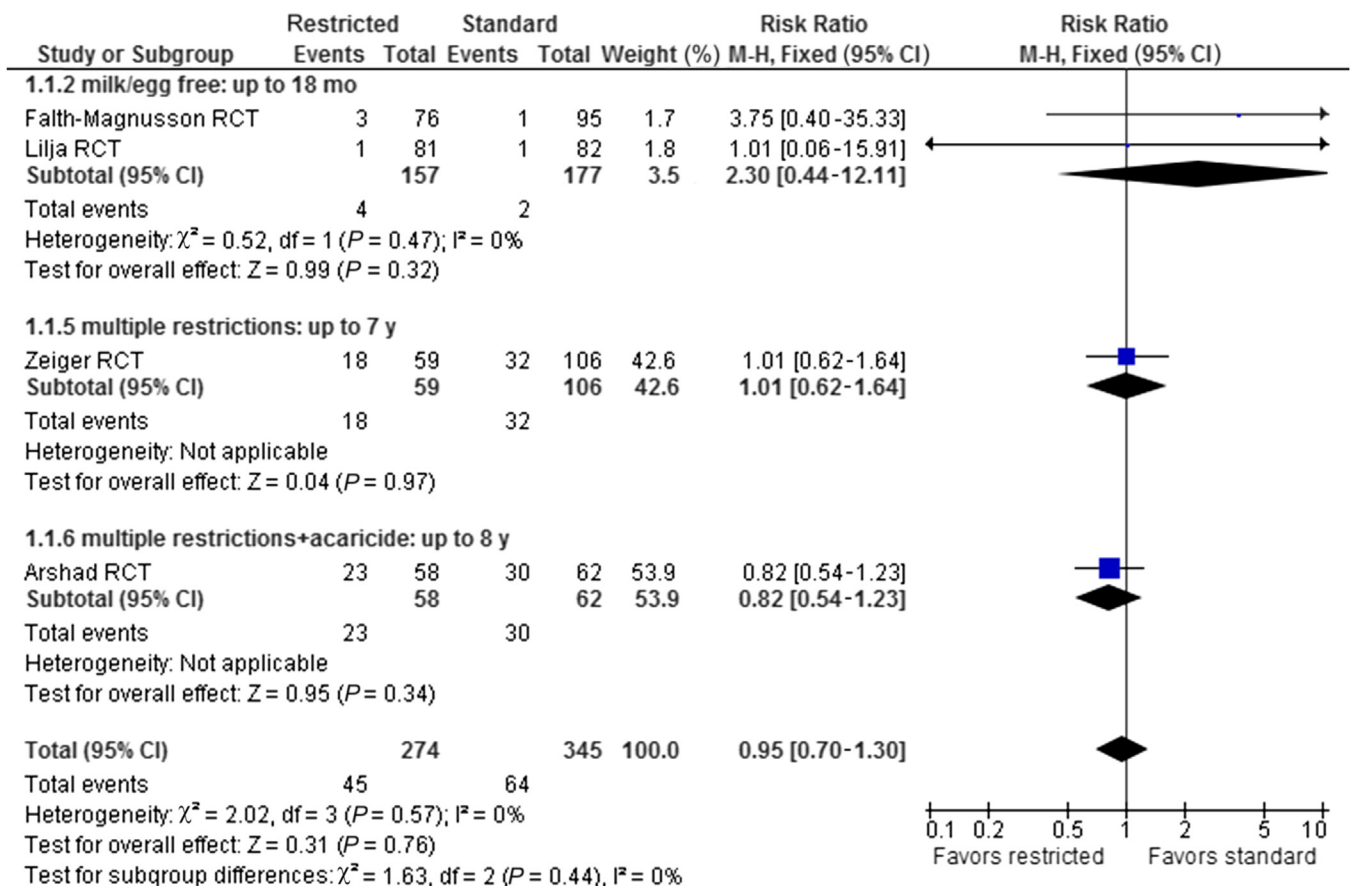


Fig. 2. Forest plot representing the meta-analysis of randomized controlled trials (RCTs) assessing the effect of maternal dietary restriction on childhood asthma.

quartiles of maternal intake of vitamin D were positively associated with allergic rhinitis in children at age 5 y. This association remained significant after adjustment for confounding variables. These results were also corrected for vitamin D supplementation.

In a study of pregnant Scottish women [58], it was reported that the mothers who consumed oily fish more than once a week during the second trimester of pregnancy ($N = 1204$; OR, 0.37; 95% CI, 0.14–0.98) were less likely to have children with hay fever at 5 y of age. No association was found between maternal cereal intake and hay fever.

Maternal diet and sensitization in children

Intervention studies. The results of three RCTs investigating maternal dietary restriction and sensitization in the offspring are shown in Figure 3. Differing interventions and timings outcome assessment precluded pooling, although each of the multiple restriction studies showed lower sensitization rates for the intervention compared with controls [34–36]. One study [26] randomly allocated women to a normal diet ($n = 108$) or one without cow's milk and egg ($n = 104$) from 28 wk gestation to birth and early lactation. No significant difference in sensitization was noted in the offspring up to 5 y of age, although the women on the milk and egg-free diet gained significantly less weight during their pregnancy than did the normal diet group. In 58 women with a family history of atopy, a restricted diet was followed during lactation, introduction of allergenic solid foods (cow's milk, soy, egg, wheat,

nut and fish) was delayed, and dust mite was controlled. At age 8 y, 37 (59.7%) children had been sensitized to one or more allergens at any time in the control group compared with 14 (25.2%) in the prophylactic group (RR, 0.40; 95% CI, 0.25–0.67) [38]. A significantly reduced rate of definite or probable food allergy in children whose mothers were in the restricted diet group compared with those from the unrestricted group (RR, 0.37; 95% CI, 0.17–0.80) was reported at 2 y, but not at 4- or 8-y follow-up [34,35].

Three other intervention studies also reported the effects of maternal dietary restriction on sensitization [29,41,42,57]. In one, no time point showed significant differences between groups for sensitization to any type of food, except for a significantly higher rate of sensitization to egg at 2 y of age in the intervention group compared with the control group (RR, 1.91; 95% CI, 1.03–3.53) [42]. The other studies [29,41] reported no significant difference in the rates of sensitization between their intervention and control groups at any of the time points measured.

The timing of the maternal dietary intervention varied although no study intervened prior to the third trimester. The type and extent of maternal dietary modifications also varied (details presented in Supplementary Table 5).

If the babies were not breast fed, five studies [26,29,34,41,42] used partly or extensively hydrolyzed formula rather than standard infant formula. The timing of introduction to solid foods and the types of solid foods that were offered also varied. In four studies [29,30,34,35], solid foods were not offered until 6 mo of

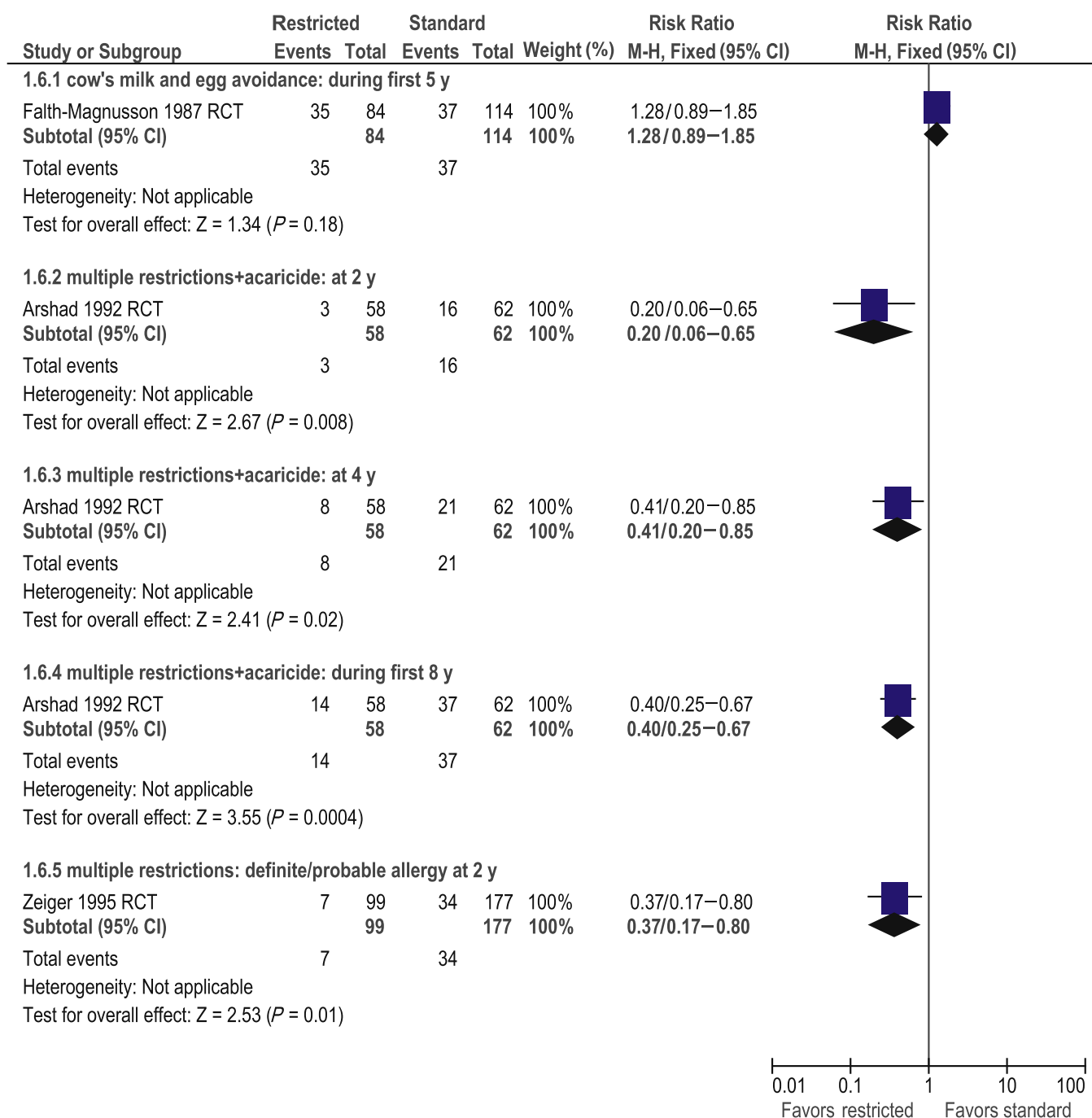


Fig. 3. Forest plot representing the meta-analysis of randomized controlled trials (RCTs) assessing the effect of maternal dietary restriction on childhood sensitization.

age, and introduction of allergenic solid foods was delayed in two of the studies [34,35] group.

Observational studies. Eight cohort studies reported the relationship between maternal food intake and sensitization to foods or aeroallergens in children as an outcome. All studies were prospective cohorts with adjusted analyses, unless otherwise stated.

Dietary associations: diet types, multiple food groups, or multiple individual foods. No studies assessed the relationship between maternal dietary types or patterns and sensitization or allergy outcomes in children younger than age 5 y.

At 5 to 7 y

Two studies [56,62] compared the type of maternal diet or patterns and sensitization or development of allergy in the offspring at 5 to 7 y.

Table 3
Summary of dietary associations by outcome*

Food type or dietary pattern	Outcome				
	Eczema	Asthma	Wheeze	Hay fever/rhinitis	Sensitization
Fruit and vegetables	Total studies: 1 [47] ↓ risk: 1 [47]	Total studies: 1 [52]	No studies	No studies	Total studies: 2 [47,53] ↓ risk: 1 [47]
Vegetables	Total studies: 3 [54,67,69] ↓ risk: 1 (green & yellow) [69]	Total studies: 2 [58, 67]	Total studies: 2 [58,64]	No studies	Total studies: 3 [54,56,76] ↓ risk: 2 (>8 servings/wk) [56] (potato) [76] ↑ risk: 1 (celery, raw sweet pepper) [54]
Fruit	Total studies: 2 [54,69] ↓ risk: 1 (apple, citrus) [69]	Total studies: 2 [55, 58] ↓ risk: 1 (apple) [55]	Total studies: 2 [58,64] ↓ risk: 1 (fruit juice) [64]	No studies	Total studies: 4 [54,56,70,76] ↑ risk: 2 (citrus; citrus intake vs inhalants [70]; total vs inhalants) [54]
Cereal	No studies	No studies	Total studies: 2 [56,64]	Total studies: 1 [55]	Total studies: 4 [56,63,70,76]
Fish	Total studies: 9 [53–55,61, 65,67,71,72,74] ↓ risk: 5 [53–55,65,72]	Total studies: 5 [48, 58,65,67,73]	Total studies: 3 [58,64,74]	No studies	Total studies: 7 [49,53,54,56,63,65,76] ↓ risk: 1 [49]
Meat	Total studies: 2 [61,71] ↑ risk: 1 [71]	Total studies: 1 [73]	Total studies: 2 [61,64] ↓ risk: 1 [61]	No studies	Total studies: 1 [56]
Eggs	Total studies: 2 [54,71]	Total studies: 1 [58]	Total studies: 2 [58,64]	No studies	Total studies: 1 [54]
Cow's milk and dairy products	Total studies: 3 [54,68,71]	Total studies: 3 [50, 58,73] ↓ risk: 1 [50]	Total studies: 3 [58,64,68] ↓ risk: 1 [68]	No studies	Total studies: 5 [54,56,59,63,76] ↑ risk: 1 (birch) [76]
Butter	Total studies: 1 [54]	Total studies: 1 [73]	Total studies: 2 [55,64]	No studies	Total studies: 3 [49,54,76] ↑ risk: 1 (wheat) [76]
Margarine	Total studies: 1 [54] ↑ risk: 1 [54]	Total studies: 1 [73]	Total studies: 1 [64]	No studies	Total studies: 3 [49,54,76] ↑ risk: 1 (wheat & birch) [76]
Vegetable oil	Total studies: 1 [54] ↑ risk: 1 [54]	Total studies: 1 [73]	No studies	No studies	Total studies: 1 [54]
Seeds	Total studies: 1 [54]	No studies	No studies	No studies	Total studies: 1 [54]
Nuts	Total studies: 1 [54]	Total studies: 1 [58] ↑ risk: 1 (daily vs. rarely) [58]	Total studies: 2 [58,64] ↑ risk: 1 (daily vs. rarely) [58]	No studies	Total studies: 2 [54,56]
Fast food	No studies	No studies	Total studies: 1 [64] ↑ risk: 1 [64]	No studies	No studies
Dietary patterns	Total studies: 3 [62,66,75]	Total studies: 3 [57, 62,66]	Total studies: 5 [57,62,64,66,75] ↓ risk: 2 ↓ risk (Medit & olive oil [64]; Western [75])	Total studies: 2 [57,62] ↓ risk: 1 (Medit diet) [57]	Total studies: 3 [56,62,76] ↓ risk: 2 (Medit [56], traditional [62]) ↑ risk: 1 (health conscious & vegetarian) [62]
Vitamin D from food	Total studies: 1 [60]	Total studies: 1 [60] ↓ risk: 1 [60]	Total studies: 1 [51] ↓ risk: 1 [51]	Total studies: 1 [60] ↓ risk: 1 [60]	No studies

Medit, Mediterranean

* Total number of studies examining each association compared with the total number showing any association. A decreased (↓) risk is one with OR < 1, and an increased (↑) risk is one with OR > 1. Where there is no up or down arrow, no effects were noted, or $P > 0.05$. For studies examining multiple food associations, the food or dietary pattern that was associated with an allergy outcome is noted.

The first study reported that a lower Mediterranean dietary score in pregnant women was associated with more atopy at 6.5 y of age (defined as sensitization or positive skin-prick testing to aeroallergens). The researchers scored the diet of 482 pregnant women by assigning positive scores to beneficial components (vegetables, legumes, fruits, nuts, cereal, fish, and dairy products) if maternal intake was above the median; a detrimental component (meat) was scored positively if intake was below the median. This association remained significant after the child's own diet was adjusted for adherence to a Mediterranean dietary pattern. No subanalysis was reported for the mother's atopic status although adjustment was made for it.

However, different results were reported in the U.K. ALSPAC (Avon Longitudinal Study of Parents and Children) study [62], which compared dietary patterns during pregnancy and two measures of atopy at age 7 y—log total serum IgE and positive skin-prick testing to dust mite, cat, and grass. No association was found between maternal dietary pattern and childhood atopy, but the health conscious and vegetarian dietary patterns were associated with increased total serum IgE compared with a traditional dietary pattern.

Dietary associations: individual foods

At 1 year

Judging by occurrence of atopic eczema and positive skin-prick testing, a decreased risk for atopy at 1 y of age, with increasing vitamin C in breast milk, which reflected maternal intake of fruits and vegetables was described [47].

The Isle of Wight study [63] reported frequency of maternal intake of common allergens during pregnancy and lactation and food hypersensitivity in the offspring at 1 and 3 y of age. However the numbers were too small to detect any differences.

Another study [60] compared a low and high intake of cow's milk and dairy foods during pregnancy and lactation. However, the data from this study could not be used for this review because it reported IgA levels and had no clinical data relating to sensitization in the offspring.

At 2 y

The German LISA (Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood) birth cohort looked at diet during pregnancy and allergic sensitization in 2641 children, defined as specific serum IgE ≥ 0.34 kU/L to egg, cow's milk, wheat, peanut, soy, codfish, house dust, cat dander,

mixed mold, and seasonal pollen allergens [54]. Several associations were found, but it should be noted that the confidence intervals are wide. Increasing maternal intake of celery (odds ratio [OR], 1.61; 95% CI, 1.07–2.41; $P < 0.05$), raw sweet pepper (OR, 1.45; 95% CI, 1.03–2.06; $P < 0.05$), and citrus fruit (OR, 1.82; 95% CI, 1.29–2.56; $P < 0.05$) were associated with increased childhood sensitization to any allergen. Increased maternal intake of deep-frying vegetable fat (OR, 1.61, 95% CI, 1.02–2.54; $P < 0.05$) and citrus (OR, 1.72; 95% CI, 1.02–2.92; $P < 0.05$) also was associated with increased sensitization to aeroallergens. Intake of celery and citrus was associated with increased sensitization to food allergens (OR, 1.85; 95% CI, 1.18–2.89; $P < 0.05$ and OR, 1.73; 95% CI, 1.18–2.53; $P < 0.05$, respectively).

At 4 y

In a study of children at age 4 y, no association with maternal fish intake during pregnancy and specific IgE levels or sensitization to house dust mite was discovered.

At 5 y

Several studies have reported atopy and sensitization in children at 5 y of age.

More sensitization to inhalant allergens was demonstrated in children of mothers who had greater fruit and vegetable intake, particularly citrus fruit during pregnancy and the first 3 mo of lactation [70]. This remained significant after adjustment. No association was found with food allergen sensitization.

As part of the DIPP (Diabetes Prediction and Prevention) Nutrition Study in Finland [76], researchers assessed the associations between maternal intake during lactation in 652 mothers and atopy in their children (measured as serum IgE sensitization to birch, cat, timothy grass, cow's milk, egg, and wheat). After adjustment, none of the dietary variables was significantly associated with sensitization to milk, egg, or timothy grass allergens.

With foods, maternal consumption of butter and butter spreads was associated with increased risk, whereas margarine and low-fat spreads were associated with decreased risk for sensitization for wheat allergen in the children. Maternal consumption of potatoes, milks, margarine, and low-fat spreads was associated with a decreased risk for sensitization to birch. For sensitization to cat allergen, the risk was decreased by maternal consumption of potatoes and increased by consumption of eggs.

In models in which all significant uncorrelated dietary variables were studied together (foods studied separately from nutrients), butters (increased risk), margarine (decreased risk), total and ω -3 polyunsaturated fatty acids, and saturated fatty acids (increased risk) were the most strongly related to wheat allergen. Potatoes (decreased risk), eggs, and vitamin C (both increased risk) remained the most significantly related to cat allergen, whereas potatoes, milks, and margarine and low-fat spreads (all decreased risk) were the most strongly related to birch allergic sensitization. Further adjustment for number of siblings at the time of child's birth, maternal age, maternal education, and pets in the house by 1 y of age did not change any of these results.

Associations between the type of fat in the maternal diet during pregnancy and allergic sensitization in 5 y olds born to allergic and non-allergic mothers were investigated [49]. Less sensitization to common food allergens at 5 y of age with more frequent intake of fish during pregnancy in non-atopic mothers but not in the offspring of atopic mothers was reported. The researchers also reported less sensitization to inhalant allergens in 5 y olds born to atopic mothers who consumed butter once a week (OR, 0.27; 95% CI, 0.10–0.73); however, this association was

not maintained for more frequent intakes (OR, 1.59; 95% CI, 0.51–4.79). In non-atopic mothers, consumption of butter once a week, but not for more frequent consumption, was associated with more inhalant sensitization in the children (OR, 1.73; 95% CI, 1.00–2.99 and OR, 0.81; 95% CI, 0.38–1.70).

At 6 and 7 y

Diet during pregnancy was studied in 482 atopic and non-atopic mothers in the Spanish island of Menorca [56]. Skin-prick testing indicated that 70 of the children were sensitized to aeroallergens. A low intake of vegetables (≤ 8 compared with > 8 servings/wk) was associated with a greater rate of sensitization to aeroallergens.

Summary of results

Eleven intervention studies were included in this review. The RCTs noted no significant difference overall in the prevalence of eczema and asthma in the children of women whose diets were free of common food allergens during pregnancy and lactation. One study [36], which had multiple interventions, including restriction of allergens in the maternal diet during lactation, delayed introduction of allergens into the child's diet, and dust mite control reported a lower rate of sensitization in the intervention group at all ages followed up. All of the RCTs testing the relationship between maternal diet and atopy outcomes were judged to be of moderate to high risk for bias, as well as low numbers of participants affecting their statistical power.

A summary of the results from the cohort studies examining the effect of maternal diet during pregnancy and lactation and atopic outcomes in their offspring is presented in Table 3. The results from 27 prospective cohort studies, 4 retrospective cohort studies, and 1 case–control study were included, involving approximately 40 000 children.

Compared with the RCTs, the prospective cohort studies looked at significantly more investigations into relationships between foods and atopic outcomes. Most studies showed no association between maternal food intake and allergy outcomes in their offspring. Maternal dietary patterns associated with less risk for allergic disease in children included Mediterranean dietary patterns, diets rich in fruits and vegetables, fish, and vitamin D-containing foods. Food patterns associated with higher risk for atopy included vegetable oils and margarine, nuts, and fast food.

Discussion

The lack of widespread and consistent influences of maternal diet on children's allergies is perhaps not surprising. Although the development of a predisposition toward allergy may be programmed early in the fetus, possibly in the first or second trimester [79], influences early in the neonatal period such as the mode of birth, feeding type, early infections, introduction to solid foods, and exposure to allergens also influence the developing immune system. Parental atopy, epigenetic factors, gut microbiota, dietary, and other environmental influences (such as pollution, tobacco smoke, and alcohol consumption) have potential to affect this programming. There is interplay between allergen exposure and other dietary components that may have the potential to influence the tendency toward atopy. This systematic review considered foods in a holistic manner rather than individual nutrients alone, aligning with messages from dietary guidelines to emphasize whole foods and dietary patterns. However, it is also useful to reflect how food-based dietary

patterns relate to the investigations of individual nutrients and findings regarding allergy outcomes, in particular related to long-chain PUFAs, antioxidants, vitamin D, and allergen avoidance.

Balance of ω -3 and ω -6 long-chain PUFAs

The types and amounts of long-chain PUFAs present in the diet have known immunomodulatory effects [80]. Diets high in ω -6 fatty acids such as vegetable oils rich in linoleic acid (18:2 ω -6) can enhance the synthesis of T-helper cell type 2 (Th2) cytokines promoting atopic responses [81]. On the other hand, diets rich in ω -3 PUFAs may alter the Th cell balance, inhibiting Th2 cell differentiation, thus moving away from development of allergy [82].

In this review, several cohort studies captured responses that may have reflected effects of differing fatty acid profiles in the diet. These included studies considering margarine, vegetable oil, and fish intake, as well as studies focusing on dietary patterns (Table 3). Four of the 10 studies investigating links between maternal fish intake (high ω -3) and eczema showed a decreased risk for associated childhood eczema; and a decreased risk for childhood asthma was seen in one of six studies. Two of the dietary profiles associated with increased total serum IgE at 7 y of age [62] (health conscious dietary and vegetarian diet patterns) were found to likely be rich in ω -6 fatty acids, particularly linoleic acid, although the diets are not described to this level of detail in the studies.

A number of clinical trials of fish oil intervention during pregnancy have reported modulation of the neonatal immune response toward a less allergenic phenotype and lower rates of eczema and sensitization in the first year of life [81,83–85]. The similarity between the cohort studies and the individual nutrient RCTs highlights the possibility that alterations in fatty acids in the food supply may be an important factor in reducing the rates of allergic disease.

Antioxidants

Foods (particularly fruits and vegetables) contain many antioxidants, including, but not limited to, vitamins C, A, and E; zinc; and selenium. Two opposing theories relate to antioxidant intake and the potential for development of atopy. The first is that dietary antioxidants are protective against oxidant damage and inflammation of airways. Decreased dietary antioxidants have been suggested as one cause of the increased prevalence of atopy in the Western world [69,86]. The opposing theory suggests that increased or excessive antioxidant intake suppresses Th1 differentiation and because of immune-regulatory mechanisms, promotes the development of a Th2 profile (toward atopy) [86].

Several cohort studies focusing on the mother's intake of foods rich in antioxidants showed protective effects against development of eczema and sensitization in their children. However, some cohort studies reported an increased risk for sensitization and others reported null findings (Table 3). None of the cohort studies found any association with maternal intake of breads and cereals (as sources of zinc) and subsequent intake of childhood atopy.

The associations between immune development and maternal fruit and vegetable intake may be partly related to their antioxidant content, although we were unable to find any RCTs using antioxidant vitamin supplements during pregnancy and lactation specifically reporting atopic outcomes in the offspring.

Note, however, that in addition to vitamins and minerals with antioxidant potential, fruits and vegetables also contain a range of phytonutrients with the potential to interact with the immune system [87].

Vitamin D

Vitamin D is a hormone with multiple biological roles, including immunoregulation. There is increasing interest in the link between low vitamin D status as a risk factor for the development of atopy, including food allergy [88]. Vitamin D status is derived from exposure to sunlight, natural food sources, vitamin D-fortified foods and dietary supplements. This review includes two studies assessing vitamin D from foods [51,60]. Some studies also showed associations between intake of cow's milk and reduced atopy. As some countries fortify cow's milk with vitamin D, such associations may indirectly reflect vitamin D intake.

One RCT evaluating the effect of vitamin D supplementation in 180 women during late pregnancy reported no difference between children in the supplemented or unsupplemented groups for wheeze, allergic disease, lung function, or allergic inflammation in the first 3 y [89]. The outcomes of other vitamin D supplementation intervention trials currently underway will provide information for future evidence-based dietary guidelines related to vitamin D in the diet and development of atopy.

Allergens in the maternal diet

Several small RCTs tested the effect of maternal avoidance of common dietary allergens during pregnancy and lactation in families with a history of atopic disease and the subsequent development of atopy in their offspring. None of the RCTs found a difference in asthma, hay fever, and rhinitis in children of women who followed restricted diets. Pooling of these RCTs found no difference in asthma and eczema in offspring of women who followed restricted diets. The only RCT to show any difference in maternal restriction of food allergens and the development of eczema in children also reduced exposure to house dust mite [36]. A difference in overall rates of sensitization in the children of the allergy-avoidance group was demonstrated in their first 8 y. One study [34] reported a significantly reduced rate of food allergy at 2 y of age, but not at other ages studied.

Some of the cohort studies compared high and low maternal intakes of common allergens and atopic outcomes in their children. For example, comparing high versus low intakes of common allergens and atopic outcomes (eczema and sensitization to food or aeroallergens) in children at 1 and 2 y of age, no difference was noted between groups for cow's milk, eggs, and nuts but less eczema was reported in the children at 1 y of age whose mothers had high fish intake [54]. The sensitization rates reported for these groups showed no differences. A similar finding was described with maternal fish intake and eczema in children [53]. Other association studies investigating intake of common allergens failed to show any relationship [71]. Overall, there were no clear patterns, but emerging trends suggest that higher intakes of fish [53,54] and nuts [58] during pregnancy may reduce allergy risk in some populations.

Differences in outcomes between allergy-avoidance intervention studies and observational studies may be related to varying study designs (as well as selected population groups

versus general population studies, and cointerventions), and low numbers leading to lack of statistical power. More work is needed to strengthen recommendations regarding the inclusion of common allergens in the maternal diet during pregnancy and lactation as this continues to cause confusion for health professionals and families. Feeding guidelines for prevention of food allergy have moved to an emphasis on promotion of induction of tolerance by inclusion of allergens early into the child's diet rather than avoidance of allergens [90,91]. Inclusion rather than exclusion of allergens in the maternal diet also may play a role in early immune programming.

Maternal diet during lactation as a treatment for allergies presenting in breastfed babies

Four trials investigating the use of maternal diet during lactation to manage known food allergy in the breastfed infant were also captured in this review. Although this is a separate issue to the etiology of allergy, allergens have been isolated in breast milk and maternal diet adjustment is commonly used to manage food allergies in a breastfed infant. The studies reviewed tested breastfeeding infants with atopic eczema for sensitization to allergens, which were then removed from the maternal diet. Maternal dietary restrictions of known allergens during lactation were associated with reduction in the infant's eczema scores. Our search did not locate any trials that evaluated maternal dietary restriction for non-IgE-mediated allergies in infancy, or for colitis, although this is common practice and an area requiring more research.

Limitations of this review

This is a difficult area to synthesize and so with data from many different sources, there were several limitations. Additionally, the “atopic march” means that children develop different symptoms as they age (eczema and food allergies when young, and then asthma and hay fever as they age). For the cohort studies, the methodology used to gather data on maternal dietary intake varied. Many studies relied on retrospective dietary recall questionnaires that are less accurate than dietary data collected prospectively. The studies were heterogeneous in terms of the atopic potential of the participants. The atopic history of the parents often was not stated, or was adjusted out in the final analysis, making comparisons difficult and possibly masking associations specific to those who have an atopic tendency.

Many studies were subsets of larger cohort studies where atopy was not always a primary consideration (e.g., the DIPP study investigating diabetes). Most of the cohort studies followed children from the same country and differences in local eating patterns may restrict the generalizability of the outcome data (e.g., one Japanese study compared low versus higher dairy food intake, but their highest quartile only consumed 280 g/d of dairy product [68]). The scoring systems used to rate Mediterranean dietary patterns varied [57,66], making direct comparisons difficult.

The primary allergic outcomes in the children were not standardized in terms of diagnostic criteria and age at follow-up or diagnosis. Some studies reported medically diagnosed outcomes using standardized criteria, often ISAAC (International Study of Asthma and Allergies in Children) criteria [2], thus enabling more accurate comparisons between studies. Others reported results of parental questionnaires as the

primary outcomes. Many of the cohort studies did not follow children beyond 1 y of age. As the natural progression of atopic disease is that different manifestations are expressed at different ages—eczema, food hypersensitivity, asthma, and then hay fever—studies should plan and fund for long-term follow-up, although it is expensive and participant drop out rates can be high. When sensitization was used as an outcome, the methods of diagnosis varied, with studies reporting outcomes of serum specific IgE measures or skin-prick test results to common allergens. Where sensitization to food allergens is reported as an outcome, it is difficult to draw clear conclusions, as positive tests may not be accompanied by allergic signs when the food is ingested. The gold standard for diagnosis of food hypersensitivity is the clinical outcome on oral challenge to the food. For large studies, this is difficult and costly.

Areas for future research

The results of this systematic review support current policy documents recommending that no specific restrictions in the maternal diet during pregnancy are indicated to prevent the development of atopic disorders in the newborn at this time [90–92].

The influence of maternal diet on childhood allergy continues to be a question addressed by researchers, particularly in the form of large cohort studies such as the Danish National Birth Cohort. We have judged that results from relevant studies published after our search cutoff date would not have substantially changed our findings and conclusions. However, some notable examples are possible attenuation of a link between high maternal fish consumption and reduced eczema risk [93]; alongside a potentially stronger association between high fish intake and decreased risk for asthma [94]. Two subsequent studies have reported links between maternal shellfish intake and increased risk for eczema [93], and also food allergy in children [95]. Associations with maternal intake of dairy products remain unclear, exemplified by one study that reported both risks and protective effects on asthma [96]. A new finding of a link between maternal consumption of artificially sweetened (but not sugar sweetened) soft drink and increased risk for asthma has been reported [97].

A well-balanced diet rich in fruits and vegetables, fish, and vitamin D-containing foods may be beneficial and should be investigated in further studies. Nutrient interactions with the immune system are complex, multifactorial, and may be related to genetic susceptibility, interactions with gut microbiota, and other dietary and environmental factors. As a single simple answer or solution is unlikely, a combination of study designs investigating individual nutrients, foods, and dietary patterns may be most useful in understanding the effect of maternal diet on allergy outcomes in the offspring. The links beginning to appear between maternal fish consumption and ω -3 long-chain PUFAs deserve further investigation in populations at high and normal risk for allergic disease.

The regular inclusion of fresh fruits and vegetables and dietary sources of vitamin D in the maternal diet also warrant further investigation. As food composition varies, data about a combination of foods, nutrients, and dietary patterns may provide the most useful information.

Additionally, any further studies should report parental atopic status, particularly the existence of maternal allergy, as well as relevant environmental variables.

Conclusion

The development of atopic disease is complex and multifactorial, depending on genetic potential along with many environmental influences. This review found no consistent link between maternal dietary intake and atopic outcomes in their children despite considering 11 intervention studies and 31 cohort studies including more than 40 000 children. Dietary patterns more likely to be associated with less risk for allergic disease include Mediterranean dietary patterns, diets rich in fruits and vegetables, fish, and vitamin D. Food patterns associated with higher risk for atopy included vegetable oils and margarine, nuts, and fast food. These findings require further evaluation.

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Supplementary data

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Appendix

Allergy search strategies

MEDLINE (and as adapted for EMBASE): From inception to end of August 2011

1. prenatal or antenatal or lactat* or breastf* or maternal or mother or pregnan*
2. intake or consumption or food or diet or wheez* or dermatitis or eczema or atop* or asthma or allerg* or food allergy sensitivity or IgE
3. 1 and 2

COCHRANE LIBRARY (last searched August 2011)

(prenatal) or (antenatal)
 (lactat*) or (breastf*) or (maternal) or (mother) or (pregnan*)
 (wheez*) or (dermatitis) or (eczema) or (atop*) or (asthma)
 (allerg*)
 (#1 OR #2)
 (#3 OR #4)
 (#5 AND #6)

DOES MATERNAL DIET DURING PREGNANCY AND LACTATION AFFECT ALLERGY OUTCOMES IN THEIR OFFSPRING? A SYSTEMATIC REVIEW OF FOOD BASED APPROACHES.

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TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN

Study details	Maternal dietary pattern/component	Effect size: aOR and 95% CI (except where stated otherwise)	P-value
Prospective and Retrospective cohort studies			
- 3-4 months age			
Saito 2010 (1) (n = 771) Diet during pregnancy OMCHS, Japan <i>ECZEMA defined as suspected atopic eczema (diagnosed by a doctor as having atopic eczema or possibly having atopic eczema)</i> <i>Low risk of bias</i>	Total dairy products	Q1 (52.7 g/day) 13/192 1.00 Q2 (126.0 g/day) 16/193 1.39 (0.62 to 3.20) Q3 (191.0 g/day) 18/193 1.63 (0.73 to 3.72) Q4 (288.3 g/day) 18/193 1.84 (0.82 to 4.27)	Ptrend = 0.13
	Eggs	Q1 (9.7 g/day) 17/192 1.00 Q2 (22.9 g/day) 15/193 0.87 (0.40 to 1.89) Q3 (40.7 g/day) 19/193 1.37 (0.66 to 2.86) Q4 (61.3 g/day) 14/193 0.73 (0.33 to 1.61)	Ptrend = 0.74
	Fish	Q1 (23.0 g/day) 14/192 1.00 Q2 (37.8 g/day) 15/193 0.93 (0.41 to 2.13) Q3 (51.4 g/day) 21/193 1.60 (0.75 to 3.51) Q4 (73.1 g/day) 15/193 1.15 (0.51 to 2.62)	Ptrend = 0.44
	Meat	Q1 (33.4 g/day) 10/192 1.00 Q2 (49.1 g/day) 14/193 1.46 (0.61 to 3.62) Q3 (63.6 g/day) 19/193 2.41 (1.06 to 5.75) Q4 (89.8 g/day) 22/193 2.59 (1.15 to 6.17)	Ptrend = 0.01
	<i>Adjusted for maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in the previous 1 month, season when data at baseline were collected, baby's older siblings, baby's sex, baby's birth weight, breastfeeding and bathing or showering infant</i>		
- First year of life/at 1 year age			
Hoppu 2005 (2) (n = 34 mothers with atopic disease) Diet during lactation Turku, FINLAND ECZEMA defined as the presence of atopic eczema during the first year of life and a positive SPT at 12 months of age Moderate risk of bias	Fruit and vegetables (specifically recommended an abundant intake of fresh fruit, berries and vegetables during breastfeeding)	OR 0.30 (0.09 to 0.94) (with increased vitamin C concentration in breast milk – attributed to dietary intake of vitamin C)	
Romieu 2007 (3) (n = 458) Menorca, SPAIN Diet during pregnancy ECZEMA defined as a medical diagnosis of eczema as reported by the parents at 1 year of age Low risk of bias	Fish – never, once per year, once per month, once per week, once per day)	0.73 (0.55 to 0.98) (per unit increase of log transformed weekly fish consumption)	0.036
	<i>Adjusted for maternal asthma, type of fish, smoking during pregnancy</i>		
Jedrychowski 2011 (4) (n = 469) Diet during pregnancy New York, USA and Krakow, POLAND ECZEMA defined as dry skin with itchy rash and typical	Fish	≤ 90 g/week (76/176): 1.00 91 – 205 g/week (69/168) 0.91 (0.59 to 1.41) > 205 g/week (38/125) 0.57 (0.35 to 0.93)	
	Fine particulate matter and environmental tobacco smoke exposure; modified by fish intake	PM _{2.5} > 53 µg/m ³ & smoking in house*: aRR 1.89 (0.99 to 2.44)	
	> 205 g/week: aIRR 0.72 (0.52 to 0.99) <i>Adjusted for maternal characteristics (age, education, atopy), duration of exclusive breastfeeding,</i>		

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

localisation, confirmed by a doctor	presence of older siblings, and damp/mouldy house, gender of child		
Low-moderate risk of bias	*PM _{2.5} = Personal Measurement of fine particulate matter IRR = incidence rate ratio		
- 2 years age			
Sausenthaler 2007 (5) (n = 2518; 446 with eczema) Diet during pregnancy LISA, Germany Eczema defined as doctor's diagnosis of allergic or atopic eczema in the past 6 months Low risk of bias	Milk (high versus low intake) High intake = more than sometimes	High: 304/1710 (17.8%) Low: 142/803 (17.7%) aOR 1.04 (0.80 to 1.34)	
	Yoghurt (high versus low intake) High intake = more than sometimes	High: 249/1370 (18.2%) Low: 197/1146 (17.2%) aOR 0.99 (0.78 to 1.27)	
	Cheese (high versus low intake) High intake = ≥ 4 times/week	High: 174/964 (18.0%) Low: 271/1551 (17.5%) aOR 0.87 (0.68 to 1.13)	
	Cream (high versus low intake) High intake = 3-4 times a week	High: 122/701 (17.4%) Low: 322/1786 (18.0%) aOR 1.02 (0.78 to 1.34)	
	Eggs (high versus low intake) High intake = 1-2 times a week	High: 318/1838 (17.3%) Low: 127/670 (19.0%) aOR 0.81 (0.62 to 1.06)	
	Butter (high versus low intake) High intake = 3-4 times a week	High: 274/1616 (17.0%) Low: 162/857 (18.9%) aOR 1.08 (0.79 to 1.46)	
	Margarine (high versus low intake) High intake = ≥ 4 times/week	High: 163/801 (20.3 %) Low: 267/1626 (16.4 %) aOR 1.49 (1.08 to 2.04)	
	Vegetable oils (high versus low intake) High intake = 3-4 times a week	High: 160/789 (20.3%) Low: 281/1703 (16.5%) aOR 1.48 (1.14 to 1.91)	
	Seeds (high versus low intake) High intake = 1-2 times a week	High: 130/622 (20.9%) Low: 311/1854 (16.8%) aOR 1.24 (0.94 to 1.64)	
	Deep-frying vegetable fat (high versus low intake) High intake = ≥ 2-3 times a month	High: 157/860 (18.3%) Low: 281/1605 (17.5%) aOR 1.10 (0.87 to 1.41)	
	Nuts (high versus low intake) High intake = 1-2 times a week	High: 92/548 (16.8%) Low: 351/1944 (18.1%) aOR 0.85 (0.63 to 1.14)	
	Raw carrots (high versus low intake) High intake = 1-2 times a week	High: 323/1773 (18.2%) Low: 120/727 (16.5%) aOR 1.12 (0.85 to 1.46)	
	Spinach (high versus low intake) High intake = ≥ 2-3 times a month	High: 270/1464 (18.4%) Low: 172/1027 (16.7%) aOR 1.26 (0.99 to 1.61)	
	Cabbage (high versus low intake) High intake = 1-2 times a week	High: 178/955 (18.6 %) Low: 268/1548 (17.3%) aOR 1.24 (0.96 to 1.59)	
	Celery (high versus low intake) High intake = ≥ 2-3 times a month	High: 68/398 (17.1%) Low: 367/2047 (17.9%) aOR 0.94 (0.67 to 1.31)	
	Raw tomatoes = 3-4 times a week	High: 133/774 (17.2%) Low: 310/1726 (18.0%) aOR 0.83 (0.63 to 1.10)	
	Raw sweet pepper (high versus low intake) High intake = ≥ 2-3 times a month	High: 309/1750 (17.7%) Low: 133/744 (17.9%) aOR 0.97 (0.75 to 1.27)	
	Salad (high versus low intake) High intake = 3-4 times a week	High: 139/797 (17.4%) Low: 305/1707 (17.9%) aOR 0.92 (0.69 to 1.22)	
	Vegetable juice (high versus low intake)	High: 96/550 (17.5%) Low: 345/1927 (17.9%)	

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

	High intake = ≥ 2-3 times a month	aOR 0.91 (0.68 to 1.22)	
	Citrus fruit (high versus low intake) High intake = 3-4 times a week	High: 157/909 (17.3%) Low: 284/1570 (18.1%) aOR 1.03 (0.78 to 1.35)	
	Apples (high versus low intake) High intake = ≥ 4 times/week	High: 150/857 (17.5%) Low: 296/1651 (17.9%) aOR 0.92 (0.72 to 1.21)	
	Exotic fruit (high versus low intake) High intake = 3-4 times a week	High: 282/1623 (17.4%) Low: 162/860 (18.8) aOR 0.85 (0.66 to 1.11)	
	Bananas (high versus low intake) High intake = ≥ 4 times/week	High: 346/1946 (17.8%) Low: 98/561 (17.5%) aOR 1.03 (0.77 to 1.38)	
	Strawberries (high versus low intake) High intake = 1-2 times a week	High: 148/857 (17.3%) Low: 295/1640 (18.0%) aOR 1.02 (0.77 to 1.35)	
	Fruit juice (high versus low intake) High intake = 3-4 times a week	High: 325/1782 (18.2%) Low: 120/722 (16.6%) aOR 1.18 (0.90 to 1.54)	
	Fish (high versus low intake) High intake = 1-2 times a week	High: 122/771 (15.8%) Low: 322/1727 (18.6%) aOR 0.75 (0.57 to 0.98)	
<i>Adjusted for study area, sex, maternal age at delivery, smoking during second or third trimester of pregnancy, parental education, exclusive breastfeeding for ≥ 4 months, family history of atopy, season of birth, and all dietary variables</i>			
Miyake 2009 (6) Prospective (n = 763 with eczema at 16-24 months) Diet during pregnancy ISAAC definition for eczema Moderate risk of bias	Fish	Q1* (23.4 g/day) 39/763 (5%) 1.00 Q2 (38.7 g/day) 35/763 (5%) 1.10 (0.59 to 2.05) Q3 (51.7 g/day) 40/763 (5%) 1.33 (0.65 to 2.72) Q4 (73.2 g/day) 28/763 (4%) 0.73 (0.30 to 1.75)	Ptrend = 0.68
	Meat	Q1 (33.8 g/day) 40/763 (5%) 1.00 Q2 (49.0 g/day) 26/763 (3%) 0.68 (0.38 to 1.21) Q3 (63.6 g/day) 32/763 (4%) 0.80 (0.46 to 1.39) Q4 (90.8 g/day) 44/763 (6%) 1.31 (0.78 to 2.22)	Ptrend = 0.28
*quartile medians in g/day energy adjusted intake <i>Adjusted for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, maternal intake of vitamins D and E during pregnancy, changes in maternal diet in previous month, season, maternal smoking during pregnancy, baby's older siblings, baby's sex, birthweight, household smoking, breastfeeding duration and time of delivery before third survey</i>			
Oien 2010 (7) Retrospective (n = 3086; 466 with eczema) Diet during pregnancy PACT, NORWAY Eczema defined as an itchy rash coming and going for at least 6 months. Moderate-high risk of bias	Fish (never or < once a week versus ≥ once per week)	Never or <once per week (n=961) OR 1.00 ≥ once per week (n = 2052) OR 1.02 (0.82 to 1.26)	p=0.88
	Vegetables (≤ once a week versus 1 to 5 times per week versus almost daily)	≤ once a week (n=275) OR 1.00 1 - 5 times / week (n= 1505) OR 0.76 (0.55 to 1.06) almost daily (n= 985) OR 0.72 (0.51 to 1.02)	p=0.11 p=0.06
	<i>The sum of n varies for the different dietary factors due to missing data.</i>		
Miyake 2010a (8) (n = 763; 18.6% with eczema) Diet during pregnancy OMCHS, Japan Eczema defined as	Total dairy products	Q1: (43.6 g/day)* 43/763 (6%) 1.00 Q2: (120.8 g/day) 22/763 (3%) 0.45 (0.25 to 0.81) Q3: (184.5 g/day) 38/763 (5%) 0.94 (0.55 to 1.59) Q4: (280.7 g/day) 39/763 (5%) 1.01 (0.59 to 1.73)	Ptrend = 0.50
	Milk	Q1: (16.1 g/day) 37/763 (5%) 1.00 Q2: (77.9 g/day) 33/763 (4%) 0.94 (0.54 to 1.63) Q3: (144.7 g/day) 35/763 (5%) 1.12 (0.65 to 1.94)	Ptrend = 0.44

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

maternal affirmation of child ever having an itchy rash which was coming and going for at least 6 months, this itchy rash at any time in the last 12 months and in any of folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes (ISAAC)		Q4: (194.0 g/day) 37/763 (5%) 1.19 (0.69 to 2.06)	
	Yoghurt	Q1: (4.4 g/day) 41/763 (6%) 1.00 Q2: (16.9 g/day) 33/763 (4%) 0.72 (0.42 to 1.23) Q3: (40.3 g/day) 33/763 (4%) 0.73 (0.42 to 1.27) Q4: (94.6 g/day) 35/763 (5%) 0.79 (0.46 to 1.37)	Ptrend = 0.41
	Cheese	Q1: (0.0 g/day) 41/763 (5%) 1.00 Q2: (2.2 g/day) 38/763 (5%) 0.79 (0.46 to 1.34) Q3: (4.5 g/day) 33/763 (4%) 0.74 (0.43 to 1.29) Q4: (12.5 g/day) 30/763 (4%) 0.67 (0.38 to 1.16)	Ptrend = 0.16
	*quartile medians in g/day energy adjusted intake		
	<i>Adjusted for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, older siblings, sex, birthweight, household smoking in same room, breastfeeding duration and age at third survey</i>		
Moderate risk of bias	Miyake 2010b (9) (n = 763; 18.6% with eczema) Diet during pregnancy OMCHS, Japan Eczema defined as maternal affirmation of child ever having an itchy rash which was coming and going for at least 6 months, this itchy rash at any time in the last 12 months and in any of folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes (ISAAC)	Total vegetables Q1 (90.9 g/day)# 45/763 (6%) 1.00 Q2 (144.4 g/day) 29/763 (4%) 0.60 (0.34 to 1.02) Q3 (189.8 g/day) 32/763 (4%) 0.61 (0.35 to 1.05) Q4 (288.4 g/day) 36/763 (5%) 0.70 (0.41 to 1.19)	Ptrend = 0.22
		Green and yellow vegetables Q1 (27.6 g/day) 54/763 (7%) 1.00 Q2 (54.9 g/day) 22/763 (3%) 0.30 (0.16 to 0.52) Q3 (77.5 g/day) 34/763 (4%) 0.53 (0.31 to 0.89) Q4 (125.8 g/day) 32/763 (4%) 0.41 (0.24 to 0.71)	Ptrend = 0.01
		Other vegetables Q1 (53.2 g/day) 39/763 (5%) 1.00 Q2 (79.3 g/day) 35/763 (5%) 0.84 (0.49-1.44) Q3 (112.7 g/day) 33/763 (4%) 0.80 (0.46-1.37) Q4 (167.2 g/day) 35/763 (5%) 0.85 (0.50-1.46)	Ptrend = 0.54
		Total fruit Q1 (49.6 g/day) 42/763 (6%) 1.00 Q2 (114.3 g/day) 36/763 (5%) 0.99 (0.58-1.68) Q3 (176.4 g/day) 34/763 (4%) 0.89 (0.52-1.52) Q4 (290.8 g/day) 30/763 (4%) 0.78 (0.45-1.35)	Ptrend = 0.34
		Apples Q1 (0.3 g/day) 40/763 (5%) 1.00 Q2 (7.6 g/day) 44/763 (6%) 1.15 (0.69-1.93) Q3 (16.7 g/day) 23/763 (3%) 0.55 (0.30-0.98) Q4 (45.0 g/day) 35/763 (5%) 0.87 (0.49-1.52)	Ptrend = 0.24
		Citrus fruit Q1 (-0.5 g/day) 49/763 (6%) 1.00 Q2 (15.2 g/day) 34/763 (4%) 0.61 (0.36 -1.02) Q3 (34.8 g/day) 31/763 (4%) 0.57 (0.33-0.98) Q4 (87.1 g/day) 28/763 (4%) 0.53 (0.30-0.93)	Ptrend = 0.03
	#quartile medians in g/day energy adjusted intake		
	<i>Adjusted for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, changes in maternal diet in previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birth weight, household smoking in same room as infant, breastfeeding duration and age of infant at survey.</i>		
	Miyake 2011b (10) (n = 763) Diet during pregnancy OMCHS, Japan ECZEMA defined as "maternal assessment of itchy rash in last 12 months" (ISAAC)	Healthy (high intake of green and yellow vegetables, seaweed, mushrooms, white vegetables, pulses, potatoes, fish, sea products, fruit and shellfish; low intake of confectionery and soft drinks) Q1 44/190 (23%) 1.00 Q2 33/191 (17%) 0.76 (0.44 to 1.28) Q3 30/191 (17%) 0.62 (0.35 to 1.07) Q4 35/191 (18%) 0.70 (0.41 to 1.20)	Ptrend = 0.14
	Moderate risk of bias	Western (high intake of vegetable oil, salt-containing seasonings, beef and pork, processed meat, eggs, chickens and white vegetables and low intake of Q1 38/190 (20%) 1.00 Q2 35/191 (18%) 0.85 (0.49 to 1.46) Q3 27/191 (14%) 0.69 (0.39 to 1.21) Q4 42/191 (22%) 1.09 (0.64 to 1.85)	Ptrend = 0.92

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

	fruit, soft drinks and confectionery)		
	Japanese (high intake of rice, miso soup, sea products, and fish)	Q1: 32/190 (17%) 1.00 Q2: 37/191 (19%) 1.15 (0.66 to 1.99) Q3: 36/190 (19%) 1.13 (0.64 to 2.00) Q4: 37/190 (19%) 1.11 (0.64 to 1.94)	Ptrend = 0.76
Adjusted for maternal age, gestation at baseline, residential municipality, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birthweight, household smoking in the same room as the infant, breastfeeding duration, and time of delivery before the third survey			
- 2.5 years age			
Shaheen 2009 (11) (n = 9516; 2509 with eczema at 2.5 years) Diet during pregnancy ALSPAC, UK Eczema defined as "itchy dry skin rash in joints and creases of his/her body (eg, behind the knees, under the arms) since he/she was 18 months old" Moderate risk of bias	Health conscious: salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish pulses, cheese, non-white bread	1.06 (0.99 to 1.12) per standard deviation of dietary pattern score	
	Traditional: vegetables, red meat, poultry	1.00 (0.95 to 1.05) per standard deviation of dietary pattern score	
	Processed: meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans	0.97 (0.91 to 1.03) per standard deviation of dietary pattern score	
	Confectionery: chocolate, sweets, biscuits, cakes, pudding	1.03 (0.97 to 1.08) per standard deviation of dietary pattern score	
	Vegetarian: meat substitutes, pulses, nuts, herbal tea	0.99 (0.94 to 1.04) per standard deviation of dietary pattern score	
Adjusted for energy intake, maximum smoked, infections, antibiotics and paracetamol use during pregnancy; maternal educational level, housing tenure, financial difficulties, pre-pregnancy body mass index, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine, sex of child, gestational age, breastfed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of food frequency questionnaire completion, birthweight, head circumference, birth length.			
- 3 years age			
Lange 2010 (12) (n = 1376; 35% with eczema) Diet during pregnancy PROJECT VIVA, USA ECZEMA defined as a parental report of a doctor's diagnosis of eczema Low risk of bias	Mediterranean diet score (0 to 9 points)	1.00 (0.94 to 1.06) per 1 point increase in score (one point if above median consumption for dairy, fish, fruit, legumes, nuts, unsaturated-to-saturated fat ratio, vegetables and whole grains; and one point if intake of red and processed meats was below the median value)	
	AHEI-P (90 point scale)	0.94 (0.82 to 1.08) per 10 points (each of the following nine components can have 10 possible points: vegetables, fruit; ratio of white to red meat; fibre; trans fat; ratio of polyunsaturated to saturated fatty acids; and folate, calcium and iron from foods)	
	Prudent pattern	0.95 (0.83 to 1.09) (fruits, tomatoes, cabbages, green leafy vegetables, poultry and fish)	
	Western pattern.	1.06 (0.93 to 1.22) (red meat, processed meat, refined grains, snacks, sweets, desserts, French fries, and pizza)	
Adjusted for child's sex, maternal race, maternal education level, household income, maternal and paternal history of eczema, presence of children < 12 years of age at home, maternal prepregnancy BMI, breastfeeding duration, and passive smoke exposure			
Miyake 2011 (13) N=582 mother infant pairs	Maternal hair mercury levels at 29-39 months	ECZEMA Risk (%) Maternal hair mercury (µg/g)	

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

OMCHS, Japan Diet during pregnancy ISAAC definition for eczema	postpartum were used as a surrogate for antenatal mercury exposure (fish)	≤ 1.09 1.10-1.51 1.52-2.10 ≥ 2.11	28/145 (19.3) 22/139 (15.8) 22/150 (14.7) 28/148 (18.9)	1.00 0.86 (0.45-1.63) 0.77 (0.40-1.45) 0.93 (0.49-1.75)	p-trend 0.74
Moderate risk of bias	Adjusted for maternal age, residential municipality at baseline, maternal and paternal education, maternal and paternal history of allergic disorders, maternal energy-adjusted fish intake during pregnancy, maternal smoking during pregnancy, number of child's older siblings, child's sex, household smoking in the same room as the child, breastfeeding and children's fish intake				
- 5 years of age					
Willers 2007 (14) (n = 1253) Diet during pregnancy Diet during pregnancy Aberdeen, SCOTLAND ECZEMA defined as parental response to ISAAC questionnaire	Total fish (never (9%) versus < once/week (21%) versus $\geq$ once/week (70%))	<u>Eczema (doctor confirmed): 380/979 (30.4%)</u> Never (n = 107) 1.00 < once/week (n = 255) 0.79 (0.47 to 1.32) $\geq$ once/week (n = 831) 0.57 (0.35 to 0.92)			Ptrend = 0.008
		<u>Current eczema medication: 191/982 (15.3%)</u> Never (n = 107) 1.00 < once/week (n = 255) 0.88 (0.46 to 1.67) $\geq$ once/week (n = 831) 0.58 (0.32 to 1.06)			Ptrend = 0.028
		<u>Ever had eczema: 406/983 (32.4%)</u> Never (n = 107) 1.00 < once/week (n = 255) 0.91 (0.54 to 1.53) $\geq$ once/week (n = 831) 0.68 (0.43 to 1.10)			Ptrend = 0.05
Low risk of bias	"No consistent linear associations were found between maternal intake of total fruit, citrus/kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products or butter versus margarine/low fat spread use and respiratory or atopic outcomes in the 5-year old children"				
	Adjusted for energy intake, maternal age, paternal social class, maternal age of leaving fulltime education, maternal smoking during pregnancy, maternal atopy, child's birth weight, child's sex, presence of older siblings, breastfeeding, smoking in the child's home				
Erkkola 2009 (15) (n = 1669; 37% eczema) Diet during pregnancy FINLAND ECZEMA defined from parental responses to ISAAC questionnaire	Vitamin D from food	Q1: (< 0.31 $\mu\text{g}/\text{MJ}$) 1.07 (0.83 to 1.39) Q2/3: (0.31-0.54 $\mu\text{g}/\text{MJ}$) 1.00 Q4: (> 0.54 $\mu\text{g}/\text{MJ}$) 0.92 (0.71 to 1.20) <u>Absolute intake (log-transformed):</u> 0.94 (0.84 to 1.04) 0.95 (0.82 to 1.09)*			
		Adjusted for sex, area of birth, duration of gestation, maternal age, maternal basic education, ,maternal smoking during pregnancy, number of siblings, parental asthma, parental allergic rhinitis, and pets inside the house before the age of 1 year *additionally adjusted for energy-adjusted maternal intake of fruits and vegetables, vitamin C, vitamin E, selenium and zinc			
Low risk of bias					
Grandjean 2010 (16) (n = 464) Faroe Islands, Denmark ECZEMA determined by paediatric assessment	Fish (as a source of PCBs and mercury)	No allergy* N = 378		atopic eczema n = 60	p-value
		PCB ($\mu\text{g}/\text{g}$ serum lipid) geometric mean, IQR			
		Antenatal	1.24 (0.83-2.0)	0.70 (0.55-1.58)	0.01
		5 years	1.17 (0.73-1.96)	0.56 (0.58*-1.85)	0.07
Moderate risk of bias		Methylmercury ($\mu\text{g}/\text{L}$ blood) geometric mean, IQR			
		Antenatal	12.8 (7.2-21.1)	13.2 (7.4-24.2)	0.80
		5 years	2.5 (1.34-4.7)	3.1 (1.41-6.7)	0.13
		*Unadjusted analyses (adjusted analyses gave similar results) ** On paper value looked implausible			
- 7 to 7.5 years age					
Shaheen 2009 (11) (n = 7693) Diet during pregnancy ALSPAC, UK ECZEMA defined as "itchy dry skin rash in joints and creases of his/her body (eg, behind	Health conscious: salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish pulses, cheese, non-white bread	1.04 (0.95 to 1.13) ^{xx}			p-value = 0.38
	Traditional: vegetables, red meat, poultry	0.99 (0.92 to 1.05)			p-value = 0.71

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)

the knees, under the arms) since he/she was 18 months old” Moderate risk of bias	Processed: meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans	0.96 (0.88 to 1.05)	p-value = 0.36
	Confectionery: chocolate, sweets, biscuits, cakes, pudding	1.03 (0.95 to 1.11)	p-value = 0.51
	Vegetarian: meat substitutes, pulses, nuts, herbal tea	1.01 (0.95 to 1.08)	p-value = 0.64
Grandjean 2010 (16) (n = 464) Faroe Islands, Denmark ECZEMA determined by paediatric assessment Moderate risk of bias	Fish (as a source of PCBs and mercury)	No allergy* N = 378 atopic eczema n = 60 PCB (µg/g serum lipid) geometric mean, IQR Antenatal 1.24 (0.83-2.0) 0.70 (0.55-1.58) 7 years 0.77 (0.44-1.39) 0.60 (0.29-1.19) Methylmercury (µg/L blood) geometric mean, IQR Antenatal 12.8 (7.2-21.1) 13.2 (7.4-24.2) 7 years 2.0 (1.00-4.6) 2.2 (1.07-4.6) *Unadjusted analyses (adjusted analyses gave similar results)	p-value 0.01 0.04 0.80 0.65

ECZEMA MANAGEMENT ARTICLES			
< 1 Year old			
Cant 1986 (17) UK N = 37 Breast fed infants with eczema aged 6 weeks to 6 months RCT (crossover trial) [plus non-randomized crossover trial designed to see if the soy substitute might have provoked symptoms in the RCT] Moderate risk of bias	Dairy foods (cow's milk) and egg Trial 1: Exclusion of cow milk, egg, chocolate, wheat, nuts, fish, beef, chicken, citrus fruits, colourings, and preservatives, with use of soya-based milk substitute for 4 weeks, <i>versus</i> same dietary exclusions for same duration (4 weeks) but substitute contained cow milk and egg, <i>versus</i> normal maternal diet (4 weeks – control period)	Trial 1: (n= 17) Non-significant reduction in eczema activity score – mean 10.8 in exclusion period; 12.2 in control period Non-significant reduction in eczema area score – mean 8.6 in exclusion period; 9.4 in control period	
	Trial 2: Phase 1. Normal diet (milk and egg containing) (2 weeks) vs exclusion diet as above (2 weeks) v normal diet (2 weeks). Phase 2. Infants with eczema scores >20% difference between groups. Exclusion	Trial 2: non RCT (n = 18): In 2 children the eczema activity score decreased by > 20% when their mothers took the exclusion diet and then increased but > 20% when their mothers returned to a normal diet; In 2 children the eczema activity scores remained unchanged when their mothers took the exclusion diet but then deteriorated when the mothers took a normal diet	

TABLE E 1 MATERNAL DIET AND ECZEMA IN CHILDREN (cont)[illegible]

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN

Study details	Maternal dietary pattern/component	Effect size: aOR and 95% CI (except where stated otherwise)	
Prospective and Retrospective cohort studies			
At 2 years of age			
Oien 2010 (7) Retrospective (n = 3086; 183 with asthma) Diet during pregnancy PACT, NORWAY Doctor Diagnosed asthma Moderate-high risk of bias	Fish	never or < once a week (n = 964) OR 1.00 ≥ once per week (n = 2061) OR 0.99 (0.72 to 1.37)	p=0.96
	Vegetables	≤ once a week (n=275) OR 1.00 1 - 5 times / week (n= 1510) OR 0.98 (0.55 to 1.69) almost daily (n= 992) OR 1.02 (0.58 to 1.81)	p=0.94 p=0.94
At 3 years of age			
Camargo 2007 (20) PROJECT VIVA, USA Diet during pregnancy (n= 416) Recurrent wheeze (positive asthma predictive index (≥ 2 wheezing attacks among children with a personal diagnosis of eczema or a parental diagnosis of asthma); Low-moderate risk of bias	Cow's milk (Vit D Fortified) Low milk (<1 cup/day) Moderate (1-1.9 cups/day) High (≥ 2 cups/day)	Recurrent wheeze in children at 3 yo None 1.00 Low 0.57 (0.27 to 1.24) Moderate 0.35 (0.16 to 0.80) High 0.45 (0.20 to 1.02)	p 0.046
	<i>Adjusted for child's sex, birthweight, income, maternal age, maternal prepregnancy BMI, passive smoke exposure, breastfeeding duration at 1 year, presence of children < 12 years of age at home, maternal history of asthma, paternal history of asthma, maternal intake of fruits and vegetables.</i>		
Fitzsimon 2007 (21) (n = 631) Diet during pregnancy Life-ways Cross-Generation cohort study, Galway, IRELAND Retrospective cohort Asthma defined as doctor diagnosed asthma (in GP notes) Moderate risk of bias	Fruit Vegetables	62/605 cases (10.2%) serves FV/day (median, range) Q1: 2.3 (0 to 3.4) 146/631 (23%) 1.00 Q2: 4.1 (3.4 to 5.0) 166/631 (26%) 1.1 (0.53 to 2.3) Q3: 6.0 (5.0 to 7.1) 146/631 (23%) 0.89 (0.39 to 2.0) Q4: 8.9 (> 7.1) 173/631 (27%) 0.50 (0.21 to 1.2)	P-value for Q4 versus Q1+2+3 = 0.07
	Fruit: (apples, pears, satsumas and mandarins, grapefruit, bananas, grapes, melons, peaches, plums and apricots, strawberries, raspberries and kiwifruit); Vegetables (carrots, spinach, broccoli, spring greens and kale, brussel sprouts, cabbage, peas, green beans and runner beans, marrow and courgettes, cauliflower, parsnips, turnips, leeks, onions, garlic, mushrooms, sweet peppers, bean sprouts, green salad and lettuce, cucumber, celery, watercress, tomatoes, sweet corn, beetroot, coleslaw, avocado) <i>Adjusted for maternal age, maternal BMI, maternal smoking during pregnancy, exposure to smoke in the home, mould or damp in home, problems with pollution in the local area, maternal university education, GMS status (medical card for low-income women), income, maternal parity, child's birthweight, child's gender, breastfeeding, fat, oily fish</i>		
Lange 2010 (12) (n = 1376; 21% with asthma) Diet during pregnancy PROJECT VIVA, USA ASTHMA defined as a parental report of	Mediterranean diet score (0 to 9 points)	1.01 (0.94 to 1.09) per 1 point increase in score (one point if above median consumption for dairy, fish, fruit, legumes, nuts, unsaturated-to-saturated fat ratio, vegetables and whole grains; and one point if intake of red and processed meats was below the median value)	
	AHEI-P (90 point scale)	1.07 (0.92 to 1.25) per 10 points (each of the following nine components can have 10 possible points: vegetables, fruit; ratio of white to red meat; fibre;	

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN (cont)

a doctor's diagnosis of asthma in the child at any time		trans fat; ratio of polyunsaturated to saturated fatty acids; and folate, calcium and iron from foods)	
	Prudent pattern	1.08 (0.93 to 1.26) (fruits, tomatoes, cabbages, green leafy vegetables, poultry and fish)	
	Western pattern	0.89 (0.76 to 1.04) (red meat, processed meat, refined grains, snacks, sweets, desserts, French fries, and pizza)	
	Adjusted for child's sex, maternal race, maternal education level, household income, maternal and paternal history of asthma, presence of children < 12 years of age at home, maternal prepregnancy BMI, breastfeeding duration, and passive smoke exposure		
At 5 years of age			
Salam 2005 (22) (n = 279 cases; 412 controls) Diet during pregnancy Children's Health Study, California, USA (nested case control study) ASTHMA defined as parental report of doctor-diagnosed asthma Low-moderate risk of bias	Oily fish	<u>Any asthma (n=279):</u> Never 1.00 Rarely 1.01 (0.54 to 1.89) At least monthly 0.80 (0.47 to 1.36) <u>Early transient asthma (47/279, 16.8%):</u> (diagnosis before 3 y, no asthma symptoms in previous 12 months or after first grade) Never 1.00* Rarely 0.68 (0.17 to 2.67) At least monthly 0.99 (0.34 to 2.87) <u>Early persistent asthma (166/279, 59.5%):</u> (diagnosis before 3 y & at least one episode of asthma or wheeze or asthma medication use in the 12 months before study entry or after starting 1 st grade) Never 1.00 Rarely 1.07 (0.53 to 2.17) At least monthly 0.45 (0.23 to 0.91) <u>Late-onset asthma (66/279, 23.7%):</u> (diagnosis after 3 y) Never 1.00 Rarely 0.80 (0.26 to 3.09) At least monthly 0.84 (0.33 to 2.12)	Ptrend = 0.40

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN (cont)

	Joint effects of maternal asthma and oily fish	<u>Any asthma:</u> NO MATERNAL ASTHMA Never 1.00 Rarely 1.31 (0.65 to 2.67) At least monthly 1.09 (0.61 to 1.94) MATERNAL ASTHMA Never 3.97 (2.07 to 7.63) Rarely 1.78 (0.54 to 5.90) At least monthly 0.81 (0.29 to 2.28) <u>Early transient asthma:</u> NO MATERNAL ASTHMA Never 1.00 Rarely 0.70 (0.16 to 3.11) At least monthly 1.38 (0.42 to 4.61) MATERNAL ASTHMA Never 3.89 (0.83 to 18.18) Rarely 1.95 (0.10 to 40.01) At least monthly 0.98 (0.12 to 7.82) <u>Early persistent asthma:</u> NO MATERNAL ASTHMA Never 1.00 Rarely 1.55 (0.68 to 3.52) At least monthly 0.62 (0.29 to 1.31) MATERNAL ASTHMA Never 5.58 (2.52 to 12.33) Rarely 2.13 (0.57 to 7.99) At least monthly 0.63 (0.16 to 2.56) <u>Late-onset asthma:</u> NO MATERNAL ASTHMA Never 1.00 Rarely 1.31 (0.65 to 2.67) At least monthly 1.09 (0.61 to 1.94) MATERNAL ASTHMA Never 6.47 (1.92 to 21.81) Rarely 8.11 (0.47 to 14.71) At least monthly 0.33 (0.04 to 2.76)	Ptrend = 0.70 Ptrend = 0.006 Pinter-action = 0.02 Ptrend = 0.67 Ptrend = 0.31 Pinter-action = 0.50 Ptrend = 0.35 Ptrend = 0.006 Pinter-action = 0.06 Ptrend = 0.42 Ptrend = 0.01 Pinter-action = 0.01
	<i>Adjusted for maternal asthma, race/ethnicity, maternal age, maternal education, gestational age, number of siblings, exclusive breastfeeding, and mutually adjusted for the other fish variable</i> <i>* Adjusted for maternal asthma, race/ethnicity, gestational age, number of siblings, exclusive breastfeeding, and mutually adjusted for the other fish variable</i>		
Willers 2007 (14) (n = 1253) Diet during pregnancy Aberdeen, SCOTLAND ASTHMA defined as parental response to ISAAC questionnaire Low risk of bias	Apples (tertiles)	<u>Asthma and wheeze in last 12 months:</u> 107/998 (8.5%) T1 (0-1/week); n = 398 1.00 T2 (1-4/week): n = 427 1.03 (0.59 to 1.80) T3 (>4/week): n = 384 0.60 (0.31 to 1.16) <u>Doctor confirmed asthma:</u> 145/998 (11.6%) T1 (0-1/week); n = 398 1.00 T2 (1-4/week): n = 427 0.83 (0.52 to 1.32) T3 (>4/week): n = 384 0.47 (0.27 to 0.82) <u>Ever had asthma:</u> 156/998 (12.5%) T1 (0-1/week); n = 398 1.00 T2 (1-4/week): n = 427 0.86 (0.54 to 1.36) T3 (>4/week): n = 384 0.54 (0.32 to 0.92)	Ptrend = 0.149 Ptrend = 0.008 Ptrend = 0.026
	"No consistent linear associations were found between maternal intake of total fruit, citrus/kiwi fruit, total vegetables, green leafy vegetables, fruit juice, whole grain products, fat from dairy products or butter versus margarine/low fat spread use and respiratory or atopic outcomes in the 5-year old children" <i>Adjusted for energy intake, maternal age, paternal social class, maternal age of leaving fulltime education,</i>		

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN (cont)

	maternal smoking during pregnancy, maternal atopy, child's birthweight, child's sex, presence of older siblings, breastfeeding, smoking in the child's home			
Erkkola 2009 (23) (n = 1669; 6% asthma) Diet during pregnancy FINLAND ASTHMA defined as persistent asthma diagnosed by a doctor, with either wheezing or asthma medication during the previous 12 months Low risk of bias	Vitamin D from food	Q1: (< 0.31µg/MJ) aHR 1.64 (1.02 to 2.64) Q2/3: (0.31-0.54 µg/MJ) aHR 1.00 Q4: (> 0.54 µg/MJ) aHR 0.81 (0.45 to 1.47) <u>Absolute intake (log-transformed):</u> aHR 0.80 (0.64 to 0.99) aHR 0.73 (0.55 to 0.95)*		
		Adjusted for sex, area of birth, duration of gestation, maternal age, maternal basic education, ,maternal smoking during pregnancy, number of siblings, parental asthma, parental allergic rhinitis, and pets inside the house before the age of 1 year *additionally adjusted for energy-adjusted maternal intake of fruits and vegetables, vitamin C, vitamin E, selenium and zinc		
Lumia 2011 (24) (n = 2679; 158 cases of asthma) Diet during pregnancy (intake in 8 th month) Turku, FINLAND ASTHMA - defined as any wheezing symptom or use of asthma medication during the preceding 12 months plus doctor diagnosed asthma validated against purchase of at least one anti-asthmatic medication during a 12 month period Similar results when allergic (1183) and non-allergic (1403) mothers were analysed separately Low risk of bias	Milk and milk products g/day	Lowest quarter (< 546.2) aHR 1.17 (0.78 to 1.77) Midhalf (546.62 to 1099.84) aHR 1 Highest quarter (> 10.99.84) aHR 0.73 (0.44 to 1.21)		Ptrend = 0.282 (aHR)
	Oils g/day	Lowest quarter (< 7.32) aHR 1.07 (0.69 to 1.65) Mid-half (7.32 to 16.60) aHR 1 Highest quarter (> 16.60) aHR 1.26 (0.82 to 1.94)		Ptrend = 0.576 (aHR)
	Margarines	User (> 15.00) aHR 0.82 (0.58 to 1.17) Non-user (0) aHR 1.00		Ptrend = 0.274 (aHR)
	Butter and butter-oil mixes g/day	Lowest quarter (< 4.63) aHR 1.41 (0.91 to 2.19) mid-half (4.63-19.78) aHR 1 highest quarter (> 19.78) aHR 1.47 (0.96-2.23)		Ptrend = 0.126 (aHR)
	Fish g/day	Lowest quarter (< 10.67) aHR 1.12 (0.74 to 1.70) mid-half (10.67-31.99) aHR 1 highest quarter (> 31.99) aHR 1.06 (0.68 to 1.65)		Ptrend = 0.861 (aHR)
	Red meat and meat products g/day	lowest quarter (< 88.49) aHR 0.76 (0.47 to 1.22) mid-half (88.49-156.44) aHR 1 highest quarter (> 156.44) aHR 1.06 (0.67 to 1.67)		Ptrend = 0.469 (aHR)
	Industrial fat mixes and animal fats g/day	lowest quarter (< 11.44) aHR 1.40 (0.91 to 2.16) mid-half (11.44- 29.70) aHR 1 highest quarter (> 29.60) aHR 1.09 (0.70 to 1.70)		Ptrend = 0.309 (aHR)
Adjusted for maternal age, mode of delivery, duration of gestation, number of earlier deliveries, birth wt, sex of child, area of birth, maternal smoking during pregnancy, parental asthma or allergic rhinitis, maternal vocational education, pets at home, farming, contact with cow stable during first year of life & duration of total breast feeding. Also adjusted for twins & siblings in the study.				
Grandjean 2010 (16) (n = 464) Faroe Islands, Denmark ASTHMA determined by paediatric assessment. Moderate risk of bias	Fish (as a source of PCBs and mercury)	No allergy* N = 378 PCB (µg/g serum lipid) geometric mean, IQR Antenatal 1.24 (0.83-2.0) 5 years 1.17 (0.73-1.96)	asthma n = 35 1.46 (0.80-2.6) 1.40 (0.63-2.7)	p-value 0.17 0.20
		Methylmercury (µg/L blood) geometric mean, IQR Antenatal 12.8 (7.2-21.1) 5 years 2.5 (1.34-4.7)	14.7 (7.6-29.2) 3.5 (1.69-10.2)	0.35 0.06
		*Unadjusted analyses (adjusted analyses gave similar results)		
At 6 to 7.5 years				
De Batlle 2008 (25) (n = 1476)	Mediterranean diet scores (high score =	Asthma (ever) n assumed to be 1326		

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN (cont)

Diet during pregnancy MEXICO Retrospective study Asthma defined as parental response to ISAAC questionnaire on respiratory and allergic symptoms	high vegetables, legumes, fruits and nuts, cereals and fish; and low dairy products, meat, junk food and fat); High versus lower score (1 st tertile versus 2 nd & 3 rd tertiles)	1.03 (0.67 to 1.56);	
Moderate –high risk of bias	Adjusted for gender of child, child’s physical exercise, current tobacco smoking at home, maternal education, maternal asthma, maternal rhinitis		
Shaheen 2009 (11) (n = 7625; 12% of children at 7.5 years) Diet during pregnancy ALSPAC, UK Asthma defined as current doctor-diagnosed asthma if mothers responded positively to the question “Has a doctor ever actually said you’re your study child has asthma?” and positively to one or both questions on wheezing and asthma in the past 12 months.	Health conscious: salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish pulses, cheese, non-white bread	0.95 (0.86 to 1.04) per standard deviation of dietary pattern score	p-value = 0.27
	Traditional: vegetables, red meat, poultry	0.96 (0.89 to 1.04) per standard deviation of dietary pattern score	p-value = 0.35
	Processed: meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans	0.98 (0.90 to 1.07) per standard deviation of dietary pattern score	p-value = 0.68
	Confectionery: chocolate, sweets, biscuits, cakes, pudding	1.00 (0.91 to 1.08) per standard deviation of dietary pattern score	p-value = 0.93
	Vegetarian: meat substitutes, pulses, nuts, herbal tea	1.02 (0.95 to 1.09) per standard deviation of dietary pattern score	p-value = 0.62
Moderate risk of bias	Adjusted for energy intake, maximum smoked, infections, antibiotics and paracetamol use during pregnancy; maternal educational level, housing tenure, financial difficulties, pre-pregnancy body mass index, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine, sex of child, gestational age, breastfed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of food frequency questionnaire completion, birthweight, head circumference, birth length, number of younger siblings and child’s BMI at age 7.		
Grandjean 2010 (16) (n = 464) Faroe Islands, Denmark ASTHMA determined by paediatric assessment.	Fish (as a source of PCBs and mercury)	No allergy* N = 378	p-value
		asthma n = 35	
Moderate risk of bias		PCB (µg/g serum lipid) geometric mean, IQR Antenatal 1.24 (0.83-2.0) 1.46 (0.80-2.6) 7 years 0.77 (0.44-1.39) 0.89 (0.49-1.70)	0.17 0.33
		Methylmercury (µg/L blood) geometric mean, IQR Antenatal 12.8 (7.2-21.1) 14.7 (7.6-29.2) 0.35 7 years 2.0 (1.00-4.6) 2.1 (1.06-3.9) 0.91	0.35 0.91
*Unadjusted analyses (adjusted analyses gave similar results)			
At 8 years			
Willers 2008 (26) (n=2 832) Diet during pregnancy Netherlands Prospective cohort (longitudinal)	Vegetables	n	Asthma Symptoms*
		Daily 2830 1 Regular + Rare 0.98 (0.84 to 1.14)	
	Fruit	Daily 2828 1 Regular + Rarely 0.91 (0.77 to 1.09)	
		Fish	Rarely 2811 1 Daily + Regularly 1.01 (0.85 to 1.20)
	Egg		Rarely 2818 1

TABLE E 2 MATERNAL DIET AND ASTHMA IN CHILDREN (cont)

Part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study		Daily + Regularly	1.03 (0.88 to 1.20)	
	Dairy	Daily	2788	1
		Regular + Rare		0.92 (0.74 to 1.15)
	Nuts	Rare	3909	1
		Daily + Regular		1.00 (0.86 to 1.17)
Low risk of bias	Nut Products	Regular v Rare		0.98 (0.84 to 1.14)
		Daily v Rare		1.47 (1.08 to 1.99)
	<i>*composite of previous three outcomes – wheeze, dyspnoea & steroid use</i> <i>The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet.</i> <i>Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).</i>			

TABLE E 3 MATERNAL DIET AND WHEEZE IN CHILDREN

Study Details	Maternal dietary pattern / component	Effect Size (aOR and 95% CI unless otherwise stated)			P value			
Prospective and Retrospective Cohorts								
Dietary associations – multiple food groups or multiple individual foods								
At 6 months to 1 year of age								
Shaheen 2009 (11) n=14,062, 8886 with wheeze. ALSPAC, UK Diet during pregnancy Moderate risk of bias	Health conscious: salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish pulses, cheese, non-white bread	Transient infant wheeze at 6 months (n = 8886) Later onset wheeze at 6 months (n = 8886) Persistent wheeze at 6 months (n = 8886)	0.98 (0.90 to 1.06) 0.93 (0.84 to 1.03) 1.00 (0.86 to 1.16)	0.57 0.19 0.99				
	Traditional: vegetables, red meat, poultry	Transient infant wheeze at 6 months (n = 8886) Later onset wheeze at 6 months (n = 8886) Persistent wheeze at 6 months (n = 8886)	0.95 (0.89 to 1.02) 1.00 (0.92 to 1.09) 0.96 (0.86 to 1.08)	0.16 0.95 0.51				
	Processed: meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans	Transient infant wheeze at 6 months (n = 8886) Later onset wheeze at 6 months (n = 8886) Persistent wheeze at 6 months (n = 8886)	0.99 (0.91 to 1.08) 1.03 (0.93 to 1.13) 1.00 (0.88 to 1.13)	0.87 0.61 0.98				
	Confectionery: chocolate, sweets, biscuits, cakes, pudding	Transient infant wheeze at 6 months (n = 8886) Later onset wheeze at 6 months (n = 8886) Persistent wheeze at 6 months (n = 8886)	1.03 (0.95 to 1.10) 0.96 (0.87 to 1.06) 1.02 (0.90 to 1.16)	0.51 0.41 0.72				
	Vegetarian: meat substitutes, pulses, nuts, herbal tea	Transient infant wheeze at 6 months (n = 8886) Later onset wheeze at 6 months (n = 8886) Persistent wheeze at 6 months (n = 8886)	1.00 (0.94 to 1.06) 0.92 (0.85 to 1.00) 1.06 (0.96 to 1.16)	0.91 0.06 0.27				
	* Adjusted for Maternal factors during pregnancy (energy intake, smoking, infections, antibiotics and paracetamol); other maternal factors (educational level, housing tenure, financial difficulties, pre-pregnancy BMI, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine); sex of child, gestational age, breast fed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of FFQ completion, birth weight, head circumference, birth length. Also number of younger siblings and child’s BMI at 7 years for later childhood outcomes.							
Castro-Rodriguez 2010 (27) n=1409 Spain EISL (International Study of Wheezing in Infants) Wheezing during first year of life. (Using ISAAC III questionnaire) Diet during pregnancy Moderate risk of bias	General diet style (Mediterranean diet score) “Pro Mediterranean’ foods (fruit, fish, vegetables, legumes, cereal, pasta, rice, potato) rated positively “Anti Mediterranean’ (meat, milk, fast foods) foods rated inversely	Wheeze (n=594) no wheeze (n=815) mean Mediterranean diet score in pregnancy, 13.1 [SD2.3] 13.3 [SD1.9]			0.036			
	Olive Oil Use	Wheeze 468/594 (78.8%) no wheeze 694/815 (85.2%)	aOR * 0.57 (0.4 to 0.9)		0.002			
	Mediterranean Diet with no olive oil	aOR=0.96 (0.8 to 1.1)			0.53			
	*Adjusted for male gender, exclusive breastfeeding, maternal asthma, day care attendance, number of people in house, number of siblings, mould stains on household walls, maternal smoking during pregnancy							
		WHEEZING (N=594)			NON WHEEZING (N=815)	P Trend		
	Frequency of other dietary components	Never / occ	1-2/wk	≥3/wk	Never /occ	1-2/wk	≥3/wk	
	Meat	1.6%	36.0%	62.4%	2.9%	33.6%	63.5%	0.22
	Hamburgers, homemade	74.1%	23.4%	2.5%	80.2%	18.1%	1.7%	0.03
	Fast food:							
	- Pizzas	63.3%	33.6%	3.1%	63.6%	33.6%	2.8%	0.95
	- Hamburgers/hotdogs	84.3%	13.7%	2.0%	86.0%	13.0%	1.0%	0.24
	- Precooked fried food	58.3%	33.8%	7.9%	62.9%	33.2%	4.0%	0.009
	White fish	16.1%	65.0%	18.9%	12.2%	69.0%	18.8%	0.11
	Oily fish	26.4%	56.4%	17.2%	23.8%	60.6%	15.6%	0.32
	Fruit, natural juice	7.0%	17.9%	75.2%	4.2%	13.8%	82.0%	0.007
	Fresh vegetables	10.9%	25.9%	63.1%	7.0%	23.9%	69.2%	0.015
salads	7.2%	21.4%	71.4%	4.5%	17.7%	77.9%	0.013	
Cooked vegetables	14.9%	39.1%	46.1%	13.6%	38.3%	48.1%	0.70	
Legumes	6.2%	55.2%	38.5%	6.1%	56.1%	37.9%	0.96	

TABLE E 3 MATERNAL DIET AND WHEEZE IN CHILDREN (cont)

	Cereals (incl bread)	6.2%	21.4%	72.4%	5.6%	18.3%	76.1%	0.31
	Pasta	9.1%	65.8%	25.1%	6.3%	70.1%	23.5%	0.10
	rice	9.5%	68.8%	21.8%	7.2%	74.9%	17.9%	0.04
	butter	64.9%	25.0%	10.1%	69.1%	22.2%	8.7%	0.27
	margarine	71.4%	20.0%	8.5%	70.2%	21.9%	7.9%	0.70
	Nuts, peanuts	60.3%	30.0%	9.7%	57.2%	33.2%	9.6%	0.47
	potatoes	11.7%	50.0%	38.3%	12.6%	50.4%	37%	0.83
	snacks	56.0%	31.7%	12.3%	57.3%	30.5%	12.2%	0.88
	milk	6.4%	8.9%	84.6%	4.1%	7.7%	88.2%	0.09
	yoghurt	10.4%	26.5%	63.2%	11.0%	22.7%	66.4%	0.28
	eggs	7.8%	68.1%	24.1%	7.3%	69.4%	23.3%	0.87
	‘industrial’ pastry	37.3%	36.4%	26.3%	40.7%	37.5%	21.8%	0.15
	alcohol	95.3%	4.3%	0.4%	97.3%	1.7%	1.0%	0.006
	Soft drinks	46.3%	34.0%	19.7%	48.5%	35.0%	16.5%	0.32
At 1-2 years								
Miyake 2009 (follow-up of Saito 2009) (6) n=763 Diet during pregnancy Wheeze in infants aged 16-24 months (ISAAC definitions) Moderate risk of bias	Meat Quartiles of maternal meat consumption during pregnancy (medians in g/day adjusted energy intake	Infant wheeze at 16-24 months (n=763) cases Q1 (33.8 g/day) 54/763 (7.1%) 1.00 Q2 (49.0 g/day) 37/763 (4.8%) 0.67 (0.40 to 1.11) Q3 (63.6 g/day) 35/763 (4.6%) 0.57 (0.33 to 0.95) Q4 (90.8 g/day) 43/763 (5.6%) 0.77 (0.47 to 1.27)						P trend 0.22
Miyake et al 2010a (8) N=763 OMCHS, Japan Diet during pregnancy Wheeze in infants (ISAAC definitions) Moderate risk of bias	Total dairy products Total dairy product intake (sum of milk, yoghurt & cheese), (medians in g/day, adjusted for energy intake)	Cases of wheeze Q1 (43.6 g/day) 50/763 (6.6%) 1 Q2 (120.8 g/day) 50/763 (6.6%) 1.04 (0.64-1.70) Q3 (184.5 g/day) 44/763 (5.8%) 0.85 (0.52-1.40) Q4 (280.7 g/day) 25/763 (3.3%) 0.45 (0.25-0.79)						0.007
	Milk	Q1 (16.1 g/day) 46/763 (6.0%) 1 Q2 (77.9 g/day) 51/763 (6.7%) 1.28 (0.79-2.10) Q3 (144.7 g/day) 47/763 (6.2%) 1.10 (0.67-1.82) Q4 (194.0 g/day) 25/763 (3.3%) 0.50 (0.28-0.87)						0.02
	Yoghurt	Q1 (4.4 g/day) 39/763 (5.1%) 1 Q2 (16.9 g/day) 39/763 (5.1%) 1.01 (0.60-1.70) Q3 (40.3 g/day) 51/763 (6.7%) 1.76 (1.05-2.98) Q4 (94.6 g/day) 40 /763 (5.2%) 1.26 (0.74-2.16)						0.15
	Cheese	Q1 (0.0 g/day) 58/763 (7.6%) 1 Q2 (2.2 g/day) 33/763 (4.3%) 0.47 (0.28-0.78) Q3 (4.5 g/d)ay 43/763 (5.6%) 0.61 (0.37-1.00) Q4 (12.5 g/day) 35/763 (4.6%) 0.51 (0.31-0.85)						0.02
Adjusted for maternal age, gestation at baseline, residential municipality at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, older siblings, sex, birthweight, household smoking in same room, breastfeeding duration and age at third survey								
Miyake et al 2011b (10) N=763 OMCHS, Japan Diet during pregnancy Wheeze in infants (ISAAC definitions) Moderate risk of bias	Maternal Dietary Patterns Healthy Pattern (high intake of green and yellow vegetables, seaweed, mushrooms, white vegetables, pulses, potatoes, fish, sea products, fruit and shellfish; low intake of confectionery and soft drinks)	Q1 48/190 (25%) 1.00 Q2 42/191 (22%) 0.80 (0.49-1.32) Q3 39/191 (20%) 0.72 (0.42-1.21) Q4 40/191 (21%) 0.68 (0.40-1.15)						0.14
	Western (high intake of vegetable oil, salt-containing seasonings, beef and pork, processed meat, eggs, chickens and white vegetables and low	Q1 51/190 (27%) 1.00 Q2 45/191 (24%) 0.72 (0.44-1.17) Q3 33/191 (17%) 0.52 (0.31-0.87) Q4 40/191 (21%) 0.59 (0.35-0.98)						0.02

TABLE E 3 MATERNAL DIET AND WHEEZE IN CHILDREN (cont)

	intake of fruit, soft drinks and confectionery)		
	Japanese (high intake of rice, miso soup, sea products, and fish)	Q1 41/190 (22%) 1.00 Q2 36/191 (19%) 0.77 (0.45-1.30) Q3 41/191 (22%) 0.94 (0.56-1.59) Q4 51/191 (27%) 1.41 (0.86-2.35)	0.12
Further control for maternal α -linolenic acid and vitamin E intake during pregnancy removed the inverse relationship between the maternal western pattern and childhood wheeze. (some numeric results were reported)			
Adjusted for maternal age, gestation at baseline, residential municipality, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, allergic rhinitis, changes in maternal diet in the previous 1 month, season when data at baseline were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birthweight, household smoking in the same room as the infant, breastfeeding duration, and time of delivery before the third survey			
At 3 years			
Lange 2010 (12) n=1376 Diet during pregnancy PROJECT VIVA, USA Recurrent wheeze at 3 years (compared with no wheeze at all in the first 3 years of life); Low risk of bias	Mediterranean diet scores	Recurrent wheeze: aOR 0.98 (0.89 to 1.08) per 1 point increase in score Mediterranean diet score (high v low): OR 0.64 (0.43 to 0.95) (one point if above median consumption for dairy, fish, fruit, legumes, nuts, unsaturated-to-saturated fat ratio, vegetables and whole grains, intake of red and processed meats below the median median value – low (0-3) v middle (4-5) v high (6-9) score.)	
	Alternate Healthy Eating Index modified for pregnancy (AHEI-P)	aOR 1.07 (0.87 to 1.30) per 10 points AHEI-P (highest v lowest quartile): OR 0.87 (0.55 to 1.37) (10 possible points for each of vegetables, fruit, ratio of white to red meat, fibre, trans fat; ratio of polyunsaturated to saturated fatty acids, folate, calcium and iron from foods – quartiles compared.)	
	Principal components analysis Prudent diet:	Prudent: aOR 1.02 (0.83 to 1.26) (fruits, tomatoes, cabbages, leafy green vegetables, poultry, fish)	
	Western diet:	Western: aOR 0.98 (0.81 to 1.19) (red meat, processed meat, refined grains, snacks, sweets, desserts, French fries and pizza.)	
	Adjusted for child's sex, maternal race, maternal education level, household income, maternal and paternal history of eczema, presence of children < 12 years of age at home, maternal prepregnancy BMI, breastfeeding duration, and passive smoke exposure		
Shaheen 2009 (11) n=14,062, 8886 with wheeze. ALSPAC, UK Diet during pregnancy Moderate risk of bias	Dietary Patterns: Health conscious	Wheezing at 3.5 years (n = 8886) 0.96 (0.88 to 1.05)	0.37
	Traditional	1.00 (0.93 to 1.07)	0.90
	Processed	1.02 (0.94 to 1.10)	0.69
	Confectionery	0.98 (0.91 to 1.06)	0.61
	Vegetarian	0.97 (0.91 to 1.04)	0.42
	* Adjusted for Maternal factors during pregnancy (energy intake, smoking, infections, antibiotics and paracetamol); other maternal factors (educational level, housing tenure, financial difficulties, pre-pregnancy BMI, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine); sex of child, gestational age, breast fed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of FFQ completion, birth weight, head circumference, birth length. Also number of younger siblings and child's BMI at 7 years for later childhood outcomes.		
Miyake et al 2011a (13) n=582 OMCHS, Japan Diet during pregnancy Wheeze (ISAAC) 29-39 months Moderate risk of bias	Fish intake (Maternal hair mercury levels at 29-39 months postpartum were used as a surrogate for antenatal mercury exposure (fish))	Risk (%) Maternal hair mercury ($\mu\text{g/g}$) ≤ 1.09 33/145 (22.8) 1.00 1.10-1.51 22/139 (15.8) 0.77 (0.41-1.44) 1.52-2.10 28/150 (18.7) 0.91 (0.50-1.64) ≥ 2.11 25/148 (16.9) 0.84 (0.45-1.55)	p-trend 0.68
	Adjusted for maternal age, residential municipality at baseline, maternal and paternal education, maternal and paternal history of allergic disorders, maternal energy-adjusted fish intake during pregnancy, maternal smoking during pregnancy, number of child's older siblings, child's sex, household smoking in the same room as the child, breastfeeding and children's		

TABLE E 3 MATERNAL DIET AND WHEEZE IN CHILDREN (cont)

		fish intake				
At 5 years						
Devereux 2007 (28) n= 1924 Scotland Diet during pregnancy Moderate risk of bias	TOTAL Maternal vitamin D intake (energy-adjusted)					
	1	2	3	4	5	
	n=213	n=246	n=237	n=261	n=255	
	Median energy-adjusted					
	Intake (IU/d)*	77	104	128	157	275
	5-95 th percentile	46-92	94-115	117-139	142-182	189-751
	Ever wheeze (n = 20.1%)					
	aOR (model 1)	1	0.84 (0.51-1.37)	0.77 (0.46-1.27)	0.65 (0.39-1.11)	0.56 (0.31-1.01)
	aOR (model 2)	1	0.86 (0.51-1.47)	0.70 (0.41-1.20)	0.57 (0.32-1.01)	0.48 (0.25-0.91)
	Wheeze in previous year (n = 12.8%)					
	aOR (model 1)	1	1.09 (0.61-1.95)	0.98 (0.54-1.80)	0.80 (0.42-1.52)	0.45 (0.21-0.97)
	aOR (model 2)	1	1.27 0.68-2.37)	0.95 (0.49-1.82)	0.70 (0.35-1.41)	0.35 (0.15-0.83)
Persistent wheeze at 2 and 5 y	aOR (model 1)	1	0.91 (0.44-1.88)	0.75 (0.35-1.61)	0.51 (0.22-1.20)	0.43 (0.16-1.12)
	aOR (model 2)	1	1.10 (0.51-2.35)	0.63 (0.27-1.45)	0.43 (0.17-1.11)	0.33 (0.11-0.98)
	Associations for maternal dietary intake were “similar” – no further results reported					
	Model 1: Adjusted for maternal atopy, maternal age, maternal smoking, maternal age at termination of fulltime education, paternal social class, deprivation index based on area of residence, breastfeeding, infant sex, infant antibiotic use in first year, birth weight, birth order, season of last menstrual period, maternal intakes of vitamin E, zinc and calcium Model 2: Additionally adjusted for energy adjusted children’s Vit D intake at 5 years.					
Willers 2007 (14) N=1212 Scotland Diet during pregnancy Low risk of bias	Fat from dairy products	no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper)				
At 6 years						
Chatzi 2008 (29) N=482 Menorca Atopic and Non atopic mothers Pregnancy Low risk of bias	Cereal ≤ 11.5 v > 11.5 serves of cereal per week	<u>Persistent wheeze at 6.5 years *</u> Low 21 (15.22%) v high 16 (11.27%)			pns	
		<u>Atopic wheeze at 6.5 years**</u> Low 14 (8.14%) v high 6 (3.51%)			pns	
	*adjusted for firstborn and lower respiratory tract infections at age 1					
	**adjusted for birth weight and maternal atopy					
De Batlle 2008 (30) n=1476 Diet during pregnancy MEXICO Retrospective study ISAAC questionnaire Moderate –high risk of bias	High versus lower Mediterranean diet scores (1 st tertile v 2 nd and 3 rd tertiles)	Age not stated but presumed to be 6-7 years <u>Wheezing (ever in child):</u> [n assumed to be 1326] aOR 0.74 (0.55 to 1.01) <u>Wheezing (currently in child):</u> [n assumed to be 1326] aOR 1.02 (0.65 to 1.60)				
At 7.5 to 8 years						
Willers 2008 (26) N= 2 832 Diet during pregnancy Netherlands Prospective cohort (longitudinal) Part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study Low risk of bias	Vegetables	n	Wheeze from 1-8 years			
		Daily	2830	1		
		Regular + Rare		0.97 (0.83 to 1.12)		
	Fruit	Daily	2828	1		
		Regular + Rarely		0.89 (0.75 to 1.04)		
	Fish	Rarely	2811	1		
		Daily + Regularly		1.10 (0.94 to 1.29)		
	Egg	Rarely	2818	1		
		Daily + Regularly		0.96 (0.84 to 1.12)		
	Dairy	Daily	2788	1		
	Regular + Rare		0.88 (0.71 to 1.09)			
Nuts	Rare	3909	1			
	Daily + Regular		0.99 (0.86 to 1.15)			
	Nut Products	Regular v Rare		1.01 (0.88 to1.18)		
		Daily v Rare		1.42 (1.06 to 1.89)		
* The child’s dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of aae were used to check for potential confounding by the child’s diet.						

TABLE E 3 MATERNAL DIET AND WHEEZE IN CHILDREN (cont)

		<i>Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).</i>	
Shaheen 2009 (11) n=14,062, 7707 with wheeze. ALSPAC, UK Diet during pregnancy Moderate risk of bias	Dietary Patterns:	<u>Wheezing at 7.5 years (n = 7707)</u>	
	Health conscious	1.00 (0.91 to 1.11)	0.94
	Traditional	1.00 (0.92 to 1.08)	0.99
	Processed	0.92 (0.84 to 1.01)	0.098
	Confectionery	1.02 (0.93 to 1.12)	0.70
	Vegetarian	1.02 (0.95 to 1.10)	0.62
<i>* Adjusted for Maternal factors during pregnancy (energy intake, smoking, infections, antibiotics and paracetamol); other maternal factors (educational level, housing tenure, financial difficulties, pre-pregnancy BMI, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine); sex of child, gestational age, breast fed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of FFQ completion, birth weight, head circumference, birth length. Also number of younger siblings and child's BMI at 7 years for later childhood outcomes.</i>			

TABLE E 4 MATERNAL DIET AND HAY FEVER OR RHINITIS IN CHILDREN

Study Details	Maternal dietary pattern / component	Effect Size (aOR and 95% CI unless otherwise stated)	P value
Trials - Avoidance Studies			
First year of life / at 1 year			
Zeiger 1989 (31); Zeiger 1995 (32) N=288 USA RCT Pregnancy Lactation Infant: when breastfeeding was supplemented or stopped Parental atopy Moderate risk of bias	Avoidance of Cow's milk Egg Peanut Concentrated soy Limited wheat Casein hydrolysate Delayed and staged introduction to solid foods Versus Standard diet in pregnancy Solid foods from 4-6 months of age Delayed milk introduction.	Allergic rhinitis: no significant differences between dietary avoidance and control groups at 4, 12 and 24 months of age 4 year follow-up: Cumulative reduction in food allergy in infancy by maternal/infant food allergen avoidance at 4 years, but the current prevalence at 4 years was similar (about 5% in each group) and failed to affect respiratory allergy development from birth to 4 years 7 year follow-up: No significant differences between groups for food allergy, atopic dermatitis, allergic rhinitis, asthma, any atopic disease, lung function or aeroallergen sensitization.	
At 5 years			
Falth-Magnusson 1987 (33) 1987a (34), 1987b(35), 1992 (36) N= 212 Sweden RCT Pregnancy (28 weeks to birth) Moderate risk of bias	Dairy foods (cow's milk) and egg Cow's milk and egg elimination from 28 weeks gestation to birth (and partially during early lactation) (n = 104 randomized) versus usual diet (typically 0.5 L milk/day and 3-5 eggs/week) (n = 108 randomized); (elimination group also had extra calcium and casein hydrolysate)	Allergic rhinoconjunctivitis (at five years); diet group 13 non-diet group 14	pns

TABLE E 4 MATERNAL DIET AND HAY FEVER OR RHINITIS IN CHILDREN (cont)

Study Details	Maternal dietary pattern / component	Effect Size (aOR and 95% CI unless otherwise stated)	P value
Prospective Cohorts. Dietary associations – multiple food groups or multiple individual foods			
At 5 years			
Willers 2007 (14) N=1212 Scotland Pregnancy – last trimester Low risk of bias	Cereals (wholegrain products)	5 year old children Whole grain products – no consistent linear associations with respiratory and atopic outcomes (exact numbers not reported in the paper).	
Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child's home at 5 years, energy intake, maternal asthma, maternal atopy, child's birth weight, child's sex, presence of older siblings, and breastfeeding			
Erkkola 2009 (15) N= 1669 Finland DIPP Study Pregnancy – 8 th month Low risk of bias	Vitamin D from food	Allergic rhinitis HR (95% CI) Absolute intake (log-transformed) 0.74 (0.57-0.96)* Energy-adjusted 0.85 (0.75-0.96)# Energy-adjusted; Model 1 0.85 (0.75-0.97)* Model 2 0.84 (0.73-0.96)* Model 3 0.79 (0.66-0.94)* Model 1 quartiles 1 st q (< 0.31µg/MJ) 1.53 (1.14-2.06)# 2 nd & 3 rd q (0.31-0.54 µg/MJ) 1 4 th q (> 0.54 µg/MJ) 0.98 (0.69-1.37)	p < 0.05 p < 0.01 p < 0.05 p < 0.05 p < 0.05 p < 0.01
(no use versus use of vitamin D supplements did not show significant differences for asthma, allergic rhinitis, or atopic eczema – adjusted for energy-adjusted maternal intake of vitamin D from food)			
At 6 -7 years of age			
De Batlle 2008 (30) N assumed to be 1326 Mexico Retrospective cohort study Pregnancy Moderate-high risk of bias	Mediterranean diet scores (high score = high vegetables, legumes, fruits and nuts, cereals and fish; and low dairy products, meat, junk food and fat); (1 st tertile v 2 nd and 3 rd tertiles)	Age not stated but presumed to be 6-7 years [n assumed to be 1326] Rhinitis (ever in child): 0.64 (0.36 to 1.15) Rhinitis (currently in child): 0.87 (0.65 to 1.18) Sneezing (currently in child): 0.71 (0.53 to 0.97) Itchy-watery eyes (currently in child): 0.96 (0.64 to 1.45)	
<i>adjusted for gender of child, physical exercise of child, current tobacco smoking at home, maternal education, maternal asthma, maternal rhinitis</i>			
Shaheen 2009 (11) UK N=14 062 Pregnancy Moderate risk of bias	Health conscious' salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish, pulses, cheese, non-white bread; 'Traditional' vegetables, red meat, poultry; 'Processed' meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans; 'Confectionery' chocolate, sweets, biscuits, cakes, puddings. 'Vegetarian' meat substitutes, pulses, nuts, herbal tea;	Hay fever at 7.5 years (673/7674) 1.00 (0.91 to 1.11) per standard deviation of dietary pattern score 1.04 (0.96 to 1.13) per standard deviation of dietary pattern score 0.93 (0.83 to 1.04) per standard deviation of dietary pattern score 1.01 (0.92 to 1.11) per standard deviation of dietary pattern score 0.97 (0.89 to 1.06) per standard deviation of dietary pattern score	
Adjusted for Maternal factors during pregnancy (energy intake, smoking, infections, antibiotics and paracetamol); other maternal factors (educational level, housing tenure, financial difficulties, pre-pregnancy BMI, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine); sex of child, gestational age, breast fed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of FFQ completion, birth weight, head circumference, birth length. Also number of younger siblings and child's BMI at 7 years for later childhood outcomes.			

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN

[illegible]

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

		allergens at any time in the control group and 14 (25.2%) in the prophylactic group (OR 0.23 95% CI 0.11 to 0.51; p < 0.001. Repeated measurement analysis confirmed significant differences: foods aOR 0.15 95% CI 0.03 to 0.80; HDM 0.07 (0.02 to 0.23) and any sensitization 0.13 (0.05 to 0.32). Any sensitization during the first 8 years of life: 37 (59.7%) 14 (25.2%) 0.23 (0.11 to 0.51)	p < 0.001.																																				
Lilja 1988 (42) N=165 Sweden RCT Maternal atopy Pregnancy 3rd trimester Moderate risk of bias	Cow's Milk Egg Four diet types* 'free'; no milk or eggs during the last three months of pregnancy (n = 37) 'reduced'; no apparent intake, but diet not completely free of milk and eggs (n = 32) 'normal'; about 0.5 L cows' milk daily and three hens' eggs weekly (n = 39) 'high'; about one L milk daily and one egg daily (n = 57)	Cord blood specific IgE (ovomucoid & betalactoglobulin) Cord blood specific IgG(ovalbumin, ovomucoid & betalactoglobulin) No significant differences between the four different maternal diet groups at birth and cord blood IgE antibodies or IgG antibodies to ovomucoid, ovalbumin and betalactoglobulin. No cord blood sIgE (ovomucoid & betalactoglobulin) was detected																																					
Lilja 1989 (43) , 1991 (44) N=162 Sweden RCT High risk families Pregnancy 3rd trimester Lactation Moderate risk of bias	Cow's Milk Egg Two diet types in pregnancy* 'reduced; no apparent intake, but diet not completely free of milk and eggs (n = 79) 'daily'; about one L milk daily and one egg daily (n = 83) After delivery 'Reduced' group was divided into two for lactation: Reduced 'A group' continued with intervention (n=25) Reduced 'B group' normal diet (n=54) Breast fed or soy formula until 6 months. Solids not until 3-4 months, No citrus, other fruits, meat, cereals and tomatoes b4 6 months. No egg or fish until 9-12 months	At 6, 12 and 18 months. SPT results (Ovalbumin, Ovomucoid, Betalactoglobulin and Cow's milk) - No difference between reduced 'A and B' groups. Serum specific IgE levels Ovomucoid, Betalactoglobulin (IgE-Ab (≥ PRU/ml)): <table><tr><td></td><td colspan="2">BF > 6 months</td><td colspan="2">BF 2- 6 months + soy formula</td><td colspan="2">BF 2- 6 months + soy formula/ cow's milk</td><td colspan="2">BF <2months + soy formula</td></tr><tr><td></td><td>R N=43</td><td>H N=45</td><td>R N=16</td><td>H N=17</td><td>R N=8</td><td>H N=5</td><td>R N=14</td><td>H N=15</td></tr><tr><td>6 months</td><td>3/38</td><td>4/45</td><td>1/14</td><td>2/17</td><td>0/7</td><td>0/5</td><td>0/13</td><td>1/13</td></tr><tr><td>18 months</td><td>9/42*</td><td>4/42</td><td>1/15</td><td>2/17</td><td>0/8</td><td>0/5</td><td>0/14</td><td>2/15</td></tr></table> R= Reduced group H = High group BF = Breast fed *P<0.05 compared to infants BF for <6 months in reduced group.		BF > 6 months		BF 2- 6 months + soy formula		BF 2- 6 months + soy formula/ cow's milk		BF <2months + soy formula			R N=43	H N=45	R N=16	H N=17	R N=8	H N=5	R N=14	H N=15	6 months	3/38	4/45	1/14	2/17	0/7	0/5	0/13	1/13	18 months	9/42*	4/42	1/15	2/17	0/8	0/5	0/14	2/15	
	BF > 6 months		BF 2- 6 months + soy formula		BF 2- 6 months + soy formula/ cow's milk		BF <2months + soy formula																																
	R N=43	H N=45	R N=16	H N=17	R N=8	H N=5	R N=14	H N=15																															
6 months	3/38	4/45	1/14	2/17	0/7	0/5	0/13	1/13																															
18 months	9/42*	4/42	1/15	2/17	0/8	0/5	0/14	2/15																															
Zeiger 1989 (31), 1995 (32) N=288 USA RCT High risk families Pregnancy 3rd trimester Lactation	Cow's Milk Egg Peanut Limited soy Limited wheat Infant - casein hydrolyzate until 12 months.	Food allergy (includes atopic dermatitis, urticaria / angioedema, and/or GI disease with specific food IgE) <table><tr><td></td><td><i>N</i></td><td><i>dietary avoidance</i></td><td><i>N</i></td><td><i>control</i></td></tr><tr><td>Food allergy (12 mo):</td><td>99</td><td></td><td>177</td><td></td></tr><tr><td>- Definite</td><td></td><td>2.0%</td><td></td><td>7.9%</td></tr><tr><td>- Probable</td><td></td><td>3.0%</td><td></td><td>8.5%</td></tr><tr><td>- TOTAL</td><td></td><td>5.0%</td><td></td><td>16.4%</td></tr></table> <i>N</i> <i>dietary avoidance</i> <i>N</i> <i>control</i>		<i>N</i>	<i>dietary avoidance</i>	<i>N</i>	<i>control</i>	Food allergy (12 mo):	99		177		- Definite		2.0%		7.9%	- Probable		3.0%		8.5%	- TOTAL		5.0%		16.4%	<i>p-value</i> 0.059 0.021 0.007											
	<i>N</i>	<i>dietary avoidance</i>	<i>N</i>	<i>control</i>																																			
Food allergy (12 mo):	99		177																																				
- Definite		2.0%		7.9%																																			
- Probable		3.0%		8.5%																																			
- TOTAL		5.0%		16.4%																																			

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Moderate risk of bias	Solid foods at 4 months of age. Cow's milk, wheat and soy delayed to 12 months Egg delayed to 24 months Fish delayed to 36 months	Food allergy (24 mo): 97 169 definite 4.1% 8.9% probable 3.1% 11.2% TOTAL 7.2% 20.1%	0.216 0.021 0.005
		Foods associated with positive challenges in the control group included egg (n = 8), milk (n = 4), peanut (n = 1) and soy (n = 1). In the dietary avoidance group, peanut (n = 2) and egg (n = 1) caused positive food challenges. 4 year follow up: Cumulative reduction in food allergy in infancy by maternal / infant food allergen avoidance at 4 years, but the current prevalence at 4 years was similar (about 5% in each group and failed to affect respiratory allergy development from birth to 4 years. 7 year follow up: No significant differences between groups for food allergy, atopic dermatitis, allergic rhinitis, asthma, any atopic disease, lung function or aeroallergen sensitizations.	
Falth-Magnusson 1987a(33), 1987b(34), 1992 (36) N=212 women from families with at least one allergic family member Pregnancy RCT Moderate risk of bias	Cow's milk and egg elimination from 28 weeks gestation to birth (and partially during early lactation) (n = 104 randomized) v usual diet (typically 0.5 L milk/day and 3-5 eggs/week) n = 108 randomized; (elimination group also had extra calcium and casein hydrolyzate)	Children at five years of age Cord blood IgE No sig. differences between groups (but babies of atopic mothers had higher IgG levels than babies of non-atopic mothers regardless of diet) Positive skin prick tests for egg and milk in infants at 6 and 18 months: Intolerance to any food item (at five years): 16/84 in the diet group and 20/114 non-diet Allergic disease (at five years) – probable or definite; 35 in the diet group and 37 in the non-diet group	pns pns pns

Other Trials - Avoidance of allergens								
Hattevig 1989 (45) (and Hattevig 1999 – 10 year follow-up) (46) N= 115 Sweden Non randomized concurrent comparison Lactation Solid foods 6 months Breast fed or casein hydrolyzate formula Moderate risk of bias	Cow's milk Eggs Fish Diet group (n = 65 infants): Non diet group (n = 50):	Adverse reactions to:						
			Age (months)	0-3	0-6	0-9	0-12	0-18
		Eggs	Diet	0	1.5%	1.5%	1.5%	7.7%
			No diet	2.0%	2.0%	2.0%	2.0%	6.0%
Cows' milk	Diet	0	3.1%	10.8%	10.8%	10.8%		
	No diet	4.0%	6.0%	14.0%	14.0%	14.0%		
Fish	Diet	0	3.1%	3.1%	3.1%	3.1%		
	No Diet	0	0	0	3.1%	3.1%		
		Adverse reactions to food (eggs, cow's milk or fish) in children at 10 years of age: 7/50 in diet group versus 8/65 in non-diet group,						
Herrmann et al 1996 (47) N=150 Germany Patient preference trial High risk families* Pregnancy 3 rd trimester +/- Lactation Staged introduction to solid foods from 18 weeks	Cow's Milk* Egg	IgE	A	B	C	HF **		
		Cow's milk sensitization						
		At 6 months	0/27	0/28	1/36	1/39		
		At 12 months	1/24	0/21	1/30	0/24		
		Egg sensitization						
		At 6 months	1/27	1/29	3/36	3/29		
		At 12 months	3/24	2/21	3/30	2/24		
		*Goat milk & sheep milk allowed as cow's milk substitutes. Looked for sensitization to these proteins, but specific IgE Negative. **Group A (n=30) Cow's milk and egg free diet during 3 rd trimester and while exclusively breast feeding						

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

High risk of bias	Group B (n=33) Cow's milk and egg free diet while exclusively breast feeding Group C (n=41) 'Prudent' diet. At least 1000ml cow's milk and 1 egg daily during pregnancy and lactation HF (n=34) Infants who were not breast fed received partially hydrolyzed (n=19) or extensively hydrolyzed (n=15) formula.
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TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Study Details	Maternal dietary pattern / component	Effect size: aOR and 95% CI (except where stated otherwise)	P-value
Dietary associations – multiple food groups or multiple individual foods			
Prospective Cohorts			
At 5 years			
Nwaru 2011 (48) n=652 Finland DIPP Nutrition Study Atopic and Non atopic mothers Lactation	Chocolate & sweets Intake by grams	Atopy (Measured as serum IgE sensitization to birch, cat, timothy grass, cow’s milk, egg, wheat) Milk allergen 1.11 (0.82 to 1.50) Egg allergen 1.22 (0.85 to 1.76) Wheat allergen 1.51 (0.98 to 2.32) Birch allergen 1.03 (0.75 to 1.41) Cat allergen 0.82 (0.51 to 1.31) Timothy grass allergen 0.73 (0.46 to 1.17)	
Low risk of bias	Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.		
At 6.5 years			
Chatzi 2008 (49) n=482 Menorca Atopic and Non atopic mothers Pregnancy	Mediterranean diet score (0 = minimal adherence to 7 = maximal adherence): high Mediterranean diet quality (4-7) v low Mediterranean diet quality (≤ 3) [dairy assumed to be protective for pregnant women; alcohol consumption not included in the score]	Atopy (sensitization to at least one aeroallergen on SPT) Results from 468/482 children Low vs High diet score 0.55 (0.32 to 0.97) Low vs High diet score additionally adjusted for child’s adherence to a Mediterranean diet 0.55 (0.31 to 0.97)	
Low risk of bias	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birthweight and maternal atopy		
At 7 years			
Shaheen 2009 (50) N=14062 UK ALSPAC Pregnancy		Log total serum IgE (n = 4819/14062)	p value
Moderate risk of bias	Health conscious: salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish pulses, cheese, non-white bread	1.07 (1.00 to 1.14) GM ratio per SD total diet score	0.041
	Traditional: vegetables, red meat, poultry	0.96 (0.91 to 1.00) GM ratio per SD total diet score	0.075
	Processed: meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans	0.97 (0.91 to 1.04) GM ratio per SD total diet score	0.39
	Confectionery: chocolate, sweets, biscuits, cakes, pudding	1.00 (0.94 to 1.06) GM ratio per SD total diet score	0.98
	Vegetarian: meat substitutes, pulses, nuts, herbal tea	1.07 (1.02 to 1.12) GM ratio per SD total diet score	0.051*
		Atopy (n=6085/14062) (positive SPT to dermatophagoides pteronyssinus, cat or grass.	
	Health conscious	0.95 (0.88 to 1.04)	0.26
	Traditional	0.98 (0.91 to 1.05)	0.54
	Processed	0.93 (0.85 to 1.01)	0.08
	Confectionery	1.07 (0.99 to 1.15)	0.09
Vegetarian	1.02 (0.96 to 1.09)	0.44	
Vegetarian	1.02 (0.96 to 1.09)	0.44	
Adjusted for energy intake, maximum smoked, infections, antibiotics and paracetamol use during pregnancy; maternal educational level, housing tenure, financial difficulties, pre-pregnancy body mass index, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine, sex of child, gestational age, breastfed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of food frequency questionnaire completion, birthweight, head circumference, birth length, number of younger siblings and child’s BMI at age 7. * Reported as 0.0051 in paper			

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Dietary associations – single foods																							
At 1 year																							
Dietary associations – cow’s milk																							
Erkkola 2005 (23) N=112 Pregnancy and lactation Low risk of bias	Milk and dairy products Low intake group as reference group compared with high intake group: Milk high intake = “more than sometimes” Yoghurt high intake = “more than sometimes” Cheese high intake = ≥ 4 times/week Cream high intake = 3-4 times/week	Recorded IgA & IgG levels.																					
		*No record of IgE levels to these allergens, and no clinical data re allergic status of children.																					
Venter 2009 (51) N=969 Portsmouth Pregnancy and lactation Moderate to high risk of bias	Cow’s milk No (< 1% of women) versus moderate (10%) versus frequent (89%) versus uncertain (1%) consumption of milk during pregnancy	Maternal Intake <table><tr><td>Milk</td><td>Never</td><td>Moderate</td><td>Frequently</td><td>Uncertain</td><td>Total FHS</td></tr><tr><td>Positive</td><td>1/2 (4)</td><td>0/97 (0)</td><td>18/831 (82)</td><td>3/7 (14)</td><td>22</td></tr><tr><td>Negative</td><td>1/2 (<1)</td><td>97/97(11)</td><td>813/831 (89)</td><td>3/7 (<1)</td><td>914</td></tr></table> Values are expressed as (n%) FHS- Food Hypersensitivity				Milk	Never	Moderate	Frequently	Uncertain	Total FHS	Positive	1/2 (4)	0/97 (0)	18/831 (82)	3/7 (14)	22	Negative	1/2 (<1)	97/97(11)	813/831 (89)	3/7 (<1)	914
Milk	Never	Moderate	Frequently	Uncertain	Total FHS																		
Positive	1/2 (4)	0/97 (0)	18/831 (82)	3/7 (14)	22																		
Negative	1/2 (<1)	97/97(11)	813/831 (89)	3/7 (<1)	914																		
Dietary associations – fruits and vegetables																							
Hoppu 2005 (2) N=34 Finland Lactation Atopy in infants defined as occurrence of both atopic eczema in first year, and a positive SPT at the age of 12 months.	Fruit and vegetables (specifically recommended an abundant intake of fresh fruits, berries and vegetables during breastfeeding)	OR 0.30 (0.09 to 0.94) (with increased vitamin C in breast milk – attributed to maternal intake of fruits and vegetables.)			P=0.038																		
Dietary associations – cereal																							
Venter 2009 (51) N=969 Portsmouth Pregnancy and lactation Moderate to high risk of bias	Cereal: wheat No (< 1% of women) versus moderate (8%) versus frequent (92%) versus uncertain (< 1%) consumption of wheat during pregnancy	Maternal Intake <table><tr><td>Wheat</td><td>Never</td><td>Moderate</td><td>Frequently</td><td>Uncertain</td><td>Total FHS</td></tr><tr><td>Positive</td><td>0/1 (0)</td><td>0/75 (0)</td><td>4/857 (100)</td><td>0/4 (0)</td><td>4</td></tr><tr><td>Negative</td><td>1/1 (<1)</td><td>75/75 (80)</td><td>853/857 (91)</td><td>4/4 (<1)</td><td>933</td></tr></table> FHS- Food Hypersensitivity				Wheat	Never	Moderate	Frequently	Uncertain	Total FHS	Positive	0/1 (0)	0/75 (0)	4/857 (100)	0/4 (0)	4	Negative	1/1 (<1)	75/75 (80)	853/857 (91)	4/4 (<1)	933
Wheat	Never	Moderate	Frequently	Uncertain	Total FHS																		
Positive	0/1 (0)	0/75 (0)	4/857 (100)	0/4 (0)	4																		
Negative	1/1 (<1)	75/75 (80)	853/857 (91)	4/4 (<1)	933																		
At 2 years																							
Sausenthaler 2007 (5) N= 2641 LISA birth cohort, Germany Pregnancy Allergic sensitization defined as specific serum IgE ≥ 0.34kU/L to egg / cow’s milk, wheat, peanut, soy, codfish, house dust, cat dander, mixed mould, seasonal pollen allergens.	low vs high intake	Any Allergen sensitization N (%)	Food Allergens	Inhalant allergens																			
	Fish high intake = 1-2 times/week	177/1458 (12.1)	133/1464 (9.1)	70/1457 (4.8)																			
		86/663 (12.8)	66/664 (9.9)	32/663 (4.8)																			
		1.02 (0.72 to 1.43)	1.01 (0.69 to 1.48)	0.94 (0.56 to 1.57)																			
	Butter	96/753 (12.7)	73/756 (9.7)	40/752 (5.3)																			
		163/1350 (12.1)	122/1354 (9.0)	63/1350 (4.7)																			
		0.97 (0.66 to 1.42)	0.93(0.60 to 1.43)	0.86 (0.48 to 1.53)																			
	Margarine	171/1378 (12.4)	131/1382 (9.5)	66/1377 (4.8)																			
		80/653 (12.3)	62/694 (8.9)	32/653 (4.8)																			
		0.85 (0.56 to 1.27)	0.80 (0.50 to 1.27)	0.93 (0.50 to 1.73)																			
	Vegetable oils	182/1465 (12.4)	138/1470 (9.4)	71/1578 (4.9)																			
		80/653 (12.3)	60/655 (9.2)	32/653 (4.8)																			
		0.88 (0.63 to 1.25)	0.91 (0.61 to 1.34)	0.89 (0.53 to 1.51)																			
	Deep frying veg. fat	161/1353 (11.9)	127/1357 (9.4)	56/1352 (4.1)																			
		98/739 (13.3)	69/742 (9.3)	45/739 (6.1)																			
		1.25 (0.92 to 1.70)	1.12 (0.79 to 1.58)	1.61 (1.02 to 2.54)	P<0.05																		
Milk	92/689 (13.4)	70/691 (10.1)	36/688 (5.2)																				
	171/1445 (11.8)	129/1450 (8.9)	67/1445 (4.6)																				
	0.93 (0.67 to 1.28)	0.95 (0.66 to 1.37)	0.95 (0.58 to 1.57)																				
Yoghurt	132/981 (13.5)	96/986 (9.7)	55/981 (5.6)																				
	132/1154 (11.4)	104/1156 (9.0)	48/1153 (4.2)																				
	0.81 (0.59 to 1.10)	0.89 (0.62 to 1.27)	0.69 (0.43 to 1.12)																				

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

	Cheese	166/1312 (12.7)	126/1315 (9.6)	66/1311 (5.0)	
		98/824 (11.9)	74/828 (8.9)	37/824 (4.5)	
		0.99 (0.72 to 1.36)	0.97 (0.68 to 1.39)	0.93 (0.57 to 1.53)	
	Eggs	71/563 (12.6)	51/566 (9.0)	30/563 (5.3)	
		192/1568 (12.2)	148/1572 (9.4)	73/1567 (4.7)	
		0.91 (0.56 to 1.28)	0.93 (0.63 to 1.38)	0.90 (0.53 to 1.53)	
	Seeds	203/1578 (12.9)	155/1585 (9.8)	77/1578 (4.9)	
		58/525 (11.0)	43/525 (8.2)	24/524 (4.6)	
		0.78 (0.53 to 1.14)	0.72 (0.47 to 1.12)	0.75 (0.42 to 1.33)	
	Nuts	209/1668 (12.5)	157/1673 (9.4)	81/1668 (4.9)	
		51/447 (11.5)	41/449 (9.1)	20/446 (4.5)	
		0.92 (0.62 to 1.34)	1.10 (0.72 to1.67)	0.84 (0.46 to 1.53)	
	Raw Carrots	83/615 (13.5)	60/618 (9.7)	31/615 (5.0)	
		180/1511 (11.9)	140/1515 (9.2)	71/1510 (4.7)	
		0.85 (0.61 to 1.18)	1.02 (0.69 to 1.49)	0.77 (0.47 to 1.28)	
	Spinach	107/861 (12.4)	85/867 (9.8)	39/860 (4.5)	
		156/1252 (12.5)	115/1253 (9.2)	63/1252 (5.0)	
		0.97 (0.71 to 1.32)	0.82 (0.58 to 1.17)	1.18 (0.73 to 1.91)	
	Cabbage	164/1295 (12.7)	126/1300 (9.7)	60/1295 (4.6)	
		100/832 (12.0)	74/834 (8.9)	43/831 (5.2)	
		0.92 (0.66 to 1.28)	0.84 (0.58 to 1.22)	1.16 (0.71 to 1.90)	
	Celery	209/1739 (12.0)	154/1746 (8.8)	82/1738 (4.7)	
		52/340 (15.3)	43/340 (12.6)	21/340 (6.2)	
		1.61 (1.07 to 2.41)	1.85 (1.18 to 2.89)	1.39 (0.74 to 2.58)	P<0.05
	Raw tomatoes	189/1476 (12.8)	147/1482 (9.9)	68/1475 (4.6)	
		75/647 (11.6)	53/648 (8.2)	35/647 (5.4)	
		0.81 (0.57 to 1.16)	0.74 (0.49 to 1.11)	1.05 (0.62 to 1.77)	
	Raw sweet pepper	65/637 (10.2)	55/642 (8.6)	18/637 (2.8)	
		196/1481 (13.2)	143/1483 (9.6)	83/1480 (5.6)	
		1.45 (1.03 to 2.06)	1.16 (0.79 to 1.69)	2.16 (1.2 to 3.9)	P<0.05
	Salad	181/1450 (12.5)	136/1457 (9.3)	72/1449 (5.0)	
		82/677 (12.1)	64/677 (9.5)	30/677 (4.4)	
		1.09 (0.76 to 1.57)	1.14 (0.76 to 1.72)	0.92 (0.52 to 1.62)	
	Vegetable juice	212/1622 (13.1)	158/1629 (9.7)	84/1621 (5.2)	
		49/482 (10.2)	39/482 (8.1)	19/482 (3.9)	
		0.78 (0.53 to 1.16)	0.85 (0.56 to 1.31)	0.85 (0.46 to 1.56)	
	Citrus fruit	150/1355 (11.1)	110/1359 (8.1)	64/1355 (4.7)	
		109/757 (14.4)	86/759 (11.3)	38/756 (5.0)	
		1.82 (1.29 to 2.56)	1.73 (1.18 to 2.53)	1.72 (1.02 to 2.92)	P<0.05
	Apples	170/1397 (12.2)	127/1402 (9.1)	72/1396 (5.2)	
		92/734 (12.5)	71/736 (9.6)	30/734 (4.1)	
		1.07 (0.77 to 1.07)	1.01 (0.70 to 1.46)	0.87 (0.52 to 1.47)	
	Exotic Fruit	97/740 (13.1)	70/745 (9.4)	41/739 (5.5)	
		162/1373 (11.8)	126/1375 (9.2)	61/1373 (4.4)	
		0.77 (0.55 to 1.07)	0.84 (0.58 to 1.23)	0.64 (0.39 to 1.07)	
	Bananas	53/484 (11.0)	39/488 (8.0)	20/484 (4.1)	
		208/1643 (12.7)	159/1646 (9.7)	82/1642 (5.0)	
		1.08 (0.75 to 1.55)	1.14 (0.75 to 1.72)	1.10 (0.63 to 1.93)	
Strawberries	168/1412 (11.9)	132/1418 (9.3)	59/1411 (4.2)		
	94/708 (13.3)	67/709 (9.4)	43/708 (6.1)		
	1.06 (0.75 to 1.51)	0.90 (0.60 to 1.34)	1.46 (0.87 to 2.47)		
Fruit Juices	73/621 (11.8)	54/625 (8.6)	33/624 (5.3)		
	190/1507 (12.6)	145/1510 (9.6)	70/1506 (4.6)		
	1.03 (0.73 to 1.46)	1.12 (0.76 to 1.65)	0.78 (0.47 to 1.30)		
Adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables					
At 3 years					
Dietary associations – cow’s milk					
Venter 2009 (51) N=969 Portsmouth Pregnancy and lactation Moderate to high risk of bias	Cow’s milk No (< 1% of women) versus moderate (10%) versus frequent (89%) versus uncertain (1%) consumption of milk during pregnancy	Maternal Intake Milk Never Moderate Frequently Uncertain Total FHS Positive 1/2 (4) 2/97 (8) 20/831 (80) 2/7 (8) 25 Negative 1/2 (<1) 95/97(10) 810/831 (89) 5/7 (<1) 933 Values are expressed as (n%) FHS- Food Hypersensitivity			

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Dietary associations – cereal								
Venter 2009 (51) N=969 Portsmouth Pregnancy and lactation Moderate to high risk of bias	Cereal: wheat							
		Maternal Intake						
	No (< 1% of women) versus moderate (8%) versus frequent (92%) versus uncertain (< 1%) consumption of wheat during pregnancy	Wheat Positive	Never 0/1 (<1)	Moderate 0/75	Frequently 4/857 (100)	Uncertain 0/4	Total FHS 4	
		Negative	1/1 (<1)	75/75 (80)	853/857 (91)	4/4 (<1)	933	
		Values are expressed as (n%) FHS- Food Hypersensitivity						
Dietary associations – fish								
Venter 2009 (51) N=969 Portsmouth Pregnancy and lactation Moderate to high risk of bias	White Fish							
		Maternal Intake						
	No versus moderate versus frequent versus uncertain consumption during pregnancy	Fish Positive	Never 0/107(<1)	Moderate 1/107	Frequently 0/107	Uncertain 0/107	Total FHS 1	
		Negative	107/107(11)	781/107(83)	44/107(5)	4/107 (<1)	936	
		Values are expressed as (n%) FHS- Food Hypersensitivity						
At 4 years								
Romieu 2007 (3) N=458 Menorca Pregnancy Atopy (at least one positive SPT to aeroallergen Dust mite, cat, grass, olive, mixed gramineae, perietaria) Low risk of bias	Fish	Specific IgE to any at 4 years 0.93 (0.59 to 1.47) (per unit increase of log transformed weekly fish consumption)				0.768		
	Fish intake as portions per week: 0, 1/52 (once per 52 weeks), ¼ (once per month), 1 (once per week) and 7 (once per day)	Specific IgE to HDM at 4 years 1.00 (0.62 to 1.62) (per unit increase of log transformed weekly fish consumption)				0.984		
	Adjusted for maternal asthma, type of fish, smoking during pregnancy							
At 5 years								
Dietary associations – cow’s milk								
Nwaru 2011 (52) n=652 Finland DIPP Nutrition Study Atopic and Non atopic mothers Lactation Low risk of bias	Dairy foods Average Intake by grams	Atopy Measured as serum IgE sensitization to birch, cat, timothy grass, cow’s milk, egg, wheat)						
		Milk allergen	1.07 (0.76 to 1.50)					
		Egg allergen	0.96 (0.67 to 1.38)					
		Wheat allergen	0.93 (0.57 to 1.50)					
		Birch allergen	0.68 (0.48 to 0.95)			p < 0.05		
		Cat allergen	1.04 (0.69 to 1.60)					
		Timothy grass allergen	1.07 (0.73 to 1.57)					
		Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.						
Dietary associations – cereals								
Nwaru 2010 (48) N=931 Finland DIPP Nutrition Study Pregnancy Lactation Low risk of bias	Total Cereals (rye, wheat, oats, barley, rice, pasta, macaroni, starches and other grains) Average intake by grams	Food allergens (sensitization to egg, cow’s milk, fish, wheat) 1.26 (0.66 to 2.43) Inhalant allergens (house dust mite, cat, timothy grass, birch) 0.94 (0.53 to 1.66)						
	Wheat	Food allergens (sensitization to egg, cow’s milk, fish, wheat) 1.20 (0.75 to 1.93) Inhalant allergens (house dust mite, cat, timothy grass, birch) 1.16 (0.77 to 1.74)						
Nwaru 2011 (52) n=652 Finland DIPP Nutrition Study Atopic and Non atopic mothers Lactation Low risk of bias	cereals Average intake by grams	Atopy (serum IgE sensitization to birch, cat, timothy grass, cows milk, egg, wheat)						
		Milk allergen	0.77 (0.48 to 1.23)					
		Egg allergen	0.73 (0.42 to 1.26)					
		Wheat allergen	0.68 (0.32 to 1.47)					
		Birch allergen	1.02 (0.67 to 1.56)					
		Cat allergen	0.70 (0.38 to 1.27)					
		Timothy grass allergen	1.06 (0.63 to 1.79)					
		Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.						

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Dietary associations – fats					
Calvani 2006 (53) N=988 (N=295 Allergic & N=693 Non Allergic mothers) Italy APAL study Pregnancy Moderate risk of bias	Butter ≤ 1 serve/month (reference) v 1 serve/week v ≥ 2-3 serves/week	Food Sensitization (positive skin prick test for raw cow’s milk and egg-white or other foods if indicated by clinical history)		ptrend	
		Allergic mothers	n/N(%)	aOR (95%CI)*	0.80
		≤ 1 serve/month	19/156 (12.2%)	1	
		1 serve/week	6/72 (8%)	0.49 (0.16 to 1.43)	
		≥2-3 serves/ week	6/49 (12.2%)	0.84 (0.26 to 2.71)	0.46
		Non Allergic mothers		aOR (95%CI)**	
		≤ 1 serve/month	29/373 (7.9%)	1	
		1 serve/week	11/168 (6.5%)	0.91 (0.37 to 2.25)	0.77
		≥2-3 serves/ week	5/86 (5.8%)	0.92 (0.27 to 3.13)	
		Inhalant sensitization (positive skin prick test for a range of allergens)			
		Allergic mothers	n/N(%)	aOR (95%CI)***	0.15
		≤ 1 serve/month	76/156 (48.7%)	1	
1 serve/week	25/72 (34.7%)	0.27 (0.10 to 0.73)			
≥2-3 serves/ week	28/49 (57.1%)	1.59 (0.51 to 4.97)	0.77		
Non Allergic mothers		aOR (95%CI)****			
≤ 1 serve/month	150/373 (40.2%)	1			
1 serve/week	88/168 (52.4%)	1.73 (1.00 to 2.99)	0.15		
≥2-3 serves/ week	37/86 (43%)	0.81 (0.38 to 1.70)			
Margarine ≤ 1 serve/month (reference) v 1 serve/week v ≥ 2-3 serves/week	Food Sensitization (positive skin prick test for raw cow’s milk and egg-white or other foods if indicated by clinical history)			ptrend	
		Allergic mothers	n/N(%)	aOR (95%CI)*	0.67
		≤ 1 serve/month	24/214 (11.2%)	1	
		1 serve/week	2/34 (5.9%)	0.26 (0.02 to 2.54)	
		≥2-3 serves/ week	4/22 (18.2%)	2.24 (0.59 to 8.49)	0.45
		Non Allergic mothers	n/N(%)	aOR(95%CI)**	
		≤ 1 serve/month	39/528 (7.4%)	1	
		1 serve/week	3/43 (7.0%)	1.63 (0.38 to 6.87)	0.85
		≥2-3 serves/ week	2/47 (4.3%)	0.51 (0.06 to 4.32)	
		Inhalant sensitization (positive skin prick test for a range of aeroallergens)			
		Allergic mothers	n/N(%)	aOR(95%CI)***	0.54
		≤ 1 serve/month	100/214 (46.7%)	1	
		1 serve/week	13/34 (38.2%)	0.39 (0.10 to 1.48)	
≥2-3 serves/ week	12/22 (54.5%)	3.02 (0.52 to 17.2)	0.54		
Non Allergic mothers		aOR(95%CI)****			
≤ 1 serve/month	229/528 (43.4%)	1			
1 serve/week	25/43 (58.1%)	1.28 (0.53 to 3.07)			
≥2-3 serves/ week	20/47 (42.6%)	0.52 (0.19 to 1.43)			
*adjusted for maternal age, occupation and eczema **adjusted for age, gestation age, maternal occupation, oculorhinitis and eczema ***adjusted for age, allergy clinics, maternal age, preterm labour, occupation, asthma, oculorhinitis and eczema ****adjusted for age, gender, number of older siblings, allergy clinics, maternal ae, number of pregnancy, maternal occupation, paternal atopy, asthma, oculorhinitis.					
Nwaru 2011 (52) n=652 Finland DIPP Nutrition Study Atopic and Non atopic mothers Lactation Low risk of bias	Dietary Fats Average Intake by grams	Atopy Measured as serum IgE sensitization to birch, cat, timothy grass, cow’s milk, egg, wheat)			
		Milk allergen	0.92 (0.60 to 1.39)		
		Egg allergen	1.42 (0.87 to 2.32)		
		Wheat allergen	1.59 (0.83 to 3.05)		
		Birch allergen	0.72 (0.47 to 1.11)		
		Cat allergen	0.77 (0.46 to 1.30)		
		Timothy grass allergen	1.18 (0.73 to 1.92)		
		Butter and Butter spreads Average Intake by grams	Milk allergen		0.92 (0.67 to 1.26)
	Egg allergen		1.37 (0.98 to 1.90)		
	Wheat allergen		2.06 (1.26 to 3.12)		
	Birch allergen		1.05 (0.79 to 1.40)		
	Cat allergen		1.01 (0.70 to 1.45)		
	Timothy grass allergen		1.23 (0.89 to 1.69)		
	Margarine and low fat spreads Average Intake by grams	Milk allergen	0.96 (0.70 to 1.31)	p < 0.05 p < 0.05	
		Egg allergen	0.80 (0.51 to 1.26)		
		Wheat allergen	0.41 (0.18 to 0.93)		
		Birch allergen	0.68 (0.47 to 0.99)		

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

		Cat allergen 0.69 (0.43 to 1.12) Timothy grass allergen 0.96 (0.66 to 1.40)	
<i>Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.</i>			
Dietary associations – fish			
Calvani 2006 (53) N=988 (N=295 Allergic & N=693 Non Allergic mothers) Italy APAL study Pregnancy Moderate risk of bias	Fish ≤ 1 serve/month (reference) v 1 serve/week v ≥ 2-3 serves/week	Food Sensitization (positive skin prick test for raw cow's milk and egg-white or other foods if indicated by clinical history) Allergic mothers n/N(%) aOR (95%CI)* ≤ 1 serve/month 7/62 (11.3%) 1 1 serve/week 16/138 (11.6%) 1.15 (0.38 to 3.47) ≥2-3 serves/ week 8/38 (9.6%) 1.13 (0.31 to 4.1) Non Allergic mothers aOR (95%CI)** ≤ 1 serve/month 20/136 (14.7%) 1 1 serve/week 16/330 (4.8%) 0.22 (0.08 to 0.55) ≥2-3 serves/ week 10/197 (5.1%) 0.23 (0.08 to 0.69)	ptrend 0.72 0.002
		Inhalant sensitization (positive skin prick test to one of 8 aeroallergens <i>Dermatophagoides pteronissinus</i> , <i>Alternaria tenuis</i> , <i>Aspergillus fumigatus</i> , mixed grass pollen, <i>Artemisia vulgaris</i> , <i>Parietaria officinalis</i> , <i>Olea europea</i> , cat dander) Allergic mothers n/N(%) aOR (95%CI)*** ≤ 1 serve/month 27/62 (43.5%) 1 1 serve/week 63/138 (50.7%) 0.89 (0.30 to 2.60) ≥2-3 serves/ week 48/83 (42.2%) 0.74 (0.23 to 2.37) Non Allergic mothers aOR (95%CI)**** ≤ 1 serve/month 69/136 (50.7%) 1 1 serve/week 137/330 (41.5%) 1.73 (0.70 to 1.30) ≥2-3 serves/ week 92/197 (43%) 0.55 (0.28 to 1.08)	0.76 0.62
		*adjusted for maternal age, occupation and eczema **adjusted for age, gestation age, maternal occupation, oculorhinitis and eczema ***adjusted for age, allergy clinics, maternal age, preterm labour, occupation, asthma, oculorhinitis and eczema ****adjusted for age, gender, number of older siblings, allergy clinics, maternal age, number of pregnancy, maternal occupation, paternal atopy, asthma, oculorhinitis.	
Nwaru 2011 (52) n=652 Finland DIPP Nutrition Study Atopic and Non atopic mothers Lactation Atopy Measured as serum IgE sensitization to birch, cat, timothy grass, cow's milk, egg, wheat) Low risk of bias	Fish and Fish Products Average Intake by grams	Milk allergen 0.80 (0.58 to 1.12) Egg allergen 0.97 (0.69 to 1.37) Wheat allergen 0.77 (0.46 to 1.31) Birch allergen 0.79 (0.58 to 1.09) Cat allergen 1.04 (0.72 to 1.51) Timothy grass allergen 0.73 (0.50 to 1.09)	
		<i>Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.</i>	
Grandjean 2010 (16) N=464 Faroe Island birth cohort No indication of maternal atopy status Pregnancy Moderate risk of bias	Seafood Fish (as a source of PCBs and mercury);	Se total IgE Conc(kUA/l) Low (<13.6) Medium(13.6-47.7) High (>47.7) PCB (µg/g serum lipid) geometric mean, IQR Antenatal 1.16 (0.73-1.79) 1.17(0.76-1.97) 1.29 (0.83-2.3) 5 years 1.00 (0.54-1.85) 1.19(0.76-1.91) 1.27 (0.81-2.2)	0.30 0.01
		Methylmercury (ug/L blood) geometric mean, IQR Antenatal 12.1 (6.6-19.4) 13.5(7.8-21.7) 13.3 (7.6 -24.7) 5 years 2.5 (1.26-4.9) 2.8(1.41-6.1) 2.5 (1.41-4.4)	0.06 0.44
		Serum Grass specific IgE concentration (kUA/l) low (≤0.35 n=425) high(>0.35 n=39) PCB (µg/g serum lipid) geometric mean, IQR Antenatal 1.22 (0.79-2.01) 1.12(0.54-2.3) 5 years 1.14 (0.69-1.94) 1.15(0.81-2.3)	0.47 0.95
		Methylmercury (ug/L blood) Antenatal 13.3 (7.6-22.5) 9.6 (6.2-12.2) 5 years 2.7 (1.35-5.2) 2.0 (1.29-3.0)	0.02 0.08

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Dietary associations – fruits and vegetables				
Nwaru 2010 (48) n=931 Finland DIPP Nutrition Study Pregnancy and first 3 months of lactation Allergic sensitization in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch) Results for 931/1175 (79.2%) children Low risk of bias	Total fruits Fruit (apple, peach, plum, prune, orange, lemon, grapefruit, mandarin, canned fruits, melons, pineapple, grapes, banana, kiwi-fruit, avocado, dried fruits, berries) and fruit and berry juices	<i>Food allergens</i> <i>Inhalant allergens</i>	0.97 (0.77 to 1.23) 1.36 (1.09 to 1.70)	
	Malaceous fruits	<i>Food allergens</i> <i>Inhalant allergens</i>	0.97 (0.84 to 1.13) 1.00 (0.87 to 1.14)	
	Citrus fruits	<i>Food allergens</i> <i>Inhalant allergens</i>	1.00 (0.92 to 1.09) 1.14 (1.05 to 1.25)	
	Berries	<i>Food allergens</i> <i>Inhalant allergens</i>	1.07 (0.92 to 1.25) 1.12 (0.88 to 1.28)	
	Juices	<i>Food allergens</i> <i>Inhalant allergens</i>	0.99 (0.90 to 1.08) 0.98 (0.90 to 1.06)	
	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education			
Nwaru 2011 (52) n=652 Finland DIPP Nutrition Study Lactation Atopic and Non atopic mothers Atopy Measured as serum IgE sensitization to birch, cat, timothy grass, cow's milk, egg, wheat) Low risk of bias	Fruits Average Intake by grams	Milk allergen Egg allergen Wheat allergen Birch allergen Cat allergen Timothy grass allergen	1.19 (0.87 to 1.63) 1.11 (0.76 to 1.63) 1.06 (0.62 to 1.83) 1.27 (0.96 to 1.69) 1.18 (0.80 to 1.74) 0.90 (0.61 to 1.32)	
	Berries	Milk allergen Egg allergen Wheat allergen Birch allergen Cat allergen Timothy grass allergen	1.12 (0.86 to 1.46) 1.05 (0.74 to 1.50) 1.22 (0.81 to 1.85) 0.74 (0.48 to 1.13) 0.70 (0.38 to 1.27) 0.98 (0.68 to 1.41)	
	Veg and roots	Milk allergen Egg allergen Wheat allergen Birch allergen Cat allergen Timothy grass allergen	0.75 (0.51 to 1.12) 1.09 (0.77 to 1.54) 0.72 (0.39 to 1.32) 0.76 (0.54 to 1.08) 0.80 (0.50 to 1.28) 0.68 (0.43 to 1.08)	
	Potatoes	Milk allergen Egg allergen Wheat allergen Birch allergen Cat allergen Timothy grass allergen	0.77 (0.53 to 1.10) 1.11 (0.80 to 1.55) 1.01 (0.63 to 1.63) 0.65 (0.45 to 0.94)* 0.55 (0.36 to 0.91)* 1.03 (0.73 to 1.46)	p < 0.05 p < 0.05
	Adjusted for gender, place of birth (southern or northern Finland), duration of gestation, maternal smoking during pregnancy, mode of delivery, parental asthma, parental allergic rhinitis, atopic eczema at 6 months of age, and exclusive breast feeding.			
At 6 to 6.5 years				
Dietary associations – cow's milk				
Chatzi 2008 (49) n=482 MENORCA Atopic and Non atopic mothers Pregnancy Low risk of bias	Dairy Food ≤ 23 v > 23 serves of nuts per week	Atopy n=70 (sensitization to at least one aeroallergen on SPT) Low 34 /70 (16.83%) High 36/70 (17.22%)		pns
	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy			
Dietary associations – cereal				
Chatzi 2008 (49) n=482 MENORCA	Cereal ≤ 11.5 v > 11.5 serves of cereal per week	Atopy n=70 (sensitization to at least one aeroallergen on SPT) Low 34/70 (17.00%) high 36/70 (17.06%)		pns

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Atopic and Non atopic mothers Pregnancy	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy		
Low risk of bias			
Chatzi 2008 (49) n=482 MENORCA	Nuts ≤ 1 v > 1 serves of nuts per week	Atopy n=70 (sensitization to at least one aeroallergen on SPT) Low 37 /70 (16.09%) High 33/70 (18.23%)	pns
Atopic and Non atopic mothers Pregnancy	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy		
Low risk of bias			
Dietary associations – fish			
Romieu 2007 (3) N=401	Fish Fish intake as portions per week: 0, 1/52 (once per 52 weeks), ¼ (once per month), 1 (once per week) and 7 (once per day)	SPT to House dust mite (HDM), Fel d 1, grass pollen, olive tree, mixed gramineae, parietaria. Specific SPT to any at 6 years 0.74 (0.5 to 1.09) (per unit increase of log transformed weekly fish consumption) Specific SPT to HDM at 6 years 0.68 (0.46 to 1.01) (per unit increase of log transformed weekly fish consumption)	0.123 0.058
Pregnancy Atopy (at least one positive SPT to aeroallergen Dust mite, cat, grass, olive, mixed gramineae, perietaria)	Adjusted for maternal asthma, type of fish, smoking during pregnancy		
Low risk of bias			
Chatzi 2008 (49) n=482 MENORCA	Fish ≤ 2.5 v > 2.5 serves of fish per week	Atopy n=70 (sensitization to at least one aeroallergen on SPT) Low 36 /70 (16.59%) high 34/70 (17.53%)	pns
Atopic and Non atopic mothers Pregnancy	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy		
Low risk of bias			
Dietary associations – meat			
Chatzi 2008 (49) n=482 MENORCA	Red Meat < 3.25 v ≥ 3.25 serves per week	Atopy n=70 (sensitization to at least one aeroallergen on SPT) Low 47 /70 (17.41%) High 23/70 (16.31%)	pns
Atopic and Non atopic mothers Pregnancy	White Meat < 2.5 v ≥ 2.5 serves per week	Low 49 /70 (16.78%) High 21/70 (17.65%)	pns
Low risk of bias	Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy		
Dietary Associations- Fruits and Vegetables			
Romieu 2007 (3) N=401 Pregnancy	Fruits and Vegetables	No observations with any association with atopy and fruit & vegetable intake. Numerical results not reported in paper	
Atopy defined as one positive SPT (HDM, cat, grass pollen, olive tree, mixed gramineae, parietaria)	Adjusted for maternal asthma, type of fish, smoking during pregnancy		
Low risk of bias			
Chatzi 2008 (49) n=482 MENORCA	Fruits ≤ 14 v > 14 serves of fruit per week	Low 45 /70 (17.65%) high 25/70 (11.98%)	pns
Atopic and Non atopic mothers	Vegetables ≤ 8 v > 8 serves of vegetables per week	Low 47/70 (21.46%) high 23 /70 (16.23%) OR 0.40 (0.22-0.72)	p<0.01

TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

Pregnancy <u>Atopy n=70</u> (sensitization to at least one aeroallergen on SPT) <i>Low risk of bias</i>	Legumes ≤ 1v > 1 serves of legumes per week	Low 49 /70 (18.35%) high 21 /70 (14.58%)	pns
<i>Adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years, total energy intake at 6.5 years, birth weight and maternal atopy</i>			
At 7 years			
Grandjean 2010 (16) N=464 Faroe Island birth cohort No indication of maternal atopy status Pregnancy Moderate risk of bias	Seafood Fish (as a source of PCBs and mercury);	Se total IgE Conc (kUA/l) Low (<13.6) Medium(13.6-47.7) High (>47.7)	
		PCB (µg/g serum lipid) geometric mean, IQR 7 years 0.66 (0.35-1.30) 0.74(0.46-1.26) 0.88 (0.56-1.47)	0.005
		Methylmercury (ug/L) 7 years 2.1 (0.95-4.5) 2.1(1.07-4.2) 2.2 (1.06-4.9)	0.37
		Serum Grass specific IgE concentration (kUA/l) low (≤0.35 n=425) high(>0.35 n=39)	
		PCB (µg/g serum lipid) geometric mean, IQR 7 years 0.75 (0.43-1.39) 0.82(0.61-1.43)	0.57
		Methylmercury (ug/L) 7 years 2.2 (1.05-4.5) 1.7 (0.76-3.0)	0.19

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TABLE E 5 MATERNAL DIET AND SENSITIZATION IN CHILDREN (cont)

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