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Timing of Introduction of Complementary Foods and Beverages and Food Allergy, Atopic Dermatitis/Eczema, Asthma, and Allergic Rhinitis: A Systematic Review

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All TEC and NESR team members, Project leads, and FEG-TEC liaisons participated in establishing the research questions, analytic framework, and study inclusion and exclusion criteria. JEO, LKE, TLP, PN, KJ, YWP, and NT developed and conducted the literature search, screened search results, and identified studies for inclusion. JEO and LKE extracted data and assessed risk of bias for included studies. NFC, KGD, MKF, FRG, NFK, DF and KSS reviewed and provided substantive feedback on all systematic review materials, including the synthesis of the body of evidence, conclusion statement,

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and grade of the strength of the evidence. JEO prepared this report and EES provided oversight. All authors critically reviewed and approved the final report. The authors declare no conflicts of interest.

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INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between timing of introduction of complementary foods and beverages (CFB) and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis? This systematic review was conducted as part of the Pregnancy and Birth to 24 Months (P/B-24) Project by USDA's Nutrition Evidence Systematic Review (NESR).

The purpose of the P/B-24 Project was to conduct a series of systematic reviews on diet and health for women who are pregnant and for infants and toddlers from birth to 24 months of age. This project was a joint initiative led by USDA and HHS, and USDA's NESR carried out all of the systematic reviews. A Federal Expert Group (FEG), a broadly representative group of Federal researchers and program leaders, also provided input throughout the P/B-24 Project. More information about the P/B-24 Project has been published[2] and is available on the NESR website: https://nesr.usda.gov/project-specific-overview-pb-24-0.

NESR, formerly known as the Nutrition Evidence Library (NEL), specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. To conduct each P/B-24 systematic review, NESR's staff worked with a Technical Expert Collaborative (TEC), which is a group of 7–8 leading subject matter experts.

NESR's systematic review methodology involves developing and prioritizing systematic review questions, searching for and selecting studies, extracting and assessing the risk of bias of data from each included study, synthesizing the evidence, developing a conclusion statement, grading the evidence underlying the conclusion statement, and recommending future research. A detailed description of the methodology used in conducting systematic reviews for the P/B-24 Project has been published[3] and is available on the NESR website: https://nesr.usda.gov/pb-24-project-methodology-0. In addition, starting on page 47, this document includes details about the methodology as it was applied to the systematic review described herein. An analytic framework that illustrates the overall scope of the question, including the population, the interventions and/or exposures, comparators, and outcomes of interest, is found on page 47. In addition, the literature search plan that was used to identify studies included in this systematic review is found on page 49.

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[2] Stoody EE, Spahn JM, Casavale KO. The Pregnancy and Birth to 24 Months Project: a series of systematic reviews on diet and health. *Am J Clin Nutr*. 2019;109(7):685S–97S. doi: 10.1093/ajcn/nqy372.
[3] Obbagy JE, Spahn JM, Wong YP, Psota TL, Spill MK, Dreibelbis C, et al. Systematic review methodology used in the Pregnancy and Birth to 24 Months Project. *Am J Clin Nutr*. 2019;109(7):698S–704S. doi: 10.1093/ajcn/nqy226.

List of abbreviations

Abbreviation	Full name
BF	Breastfed
CF	Complementary feeding
CFB	Complementary foods and beverages
FEG	Federal Expert Group
FF	Formula fed
HHS	Department of Health and Human Services
IgE	Immunoglobulin E
NEL	Nutrition Evidence Library
NESR	Nutrition Evidence Systematic Review
NIH	National Institutes of Health
P/B-24	Pregnancy and Birth to 24 Months Project
RCT	Randomized controlled trial
TEC	Technical Expert Collaborative
USDA	United States Department of Agriculture

WHAT IS THE RELATIONSHIP BETWEEN TIMING OF INTRODUCTION OF COMPLEMENTARY FOODS AND BEVERAGES (CFB) AND FOOD ALLERGY, ATOPIC DERMATITIS/ECZEMA, ASTHMA, AND ALLERGIC RHINITIS?

PLAIN LANGUAGE SUMMARY

What is the question?

- The question is: What is the relationship between timing of introduction of complementary foods and beverages and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis?

What is the answer to the question?

- Moderate evidence suggests that there is no relationship between the age at which complementary feeding first begins and risk of developing food allergy, atopic dermatitis/eczema, or asthma during childhood.
- There is insufficient evidence to determine the relationship between the age at which complementary foods or beverages are first introduced and risk of developing allergic rhinitis during childhood.

Why was this question asked?

- This important public health question was identified and prioritized as part of the U.S. Department of Agriculture and Department of Health and Human Services Pregnancy and Birth to 24 Months Project.

How was this question answered?

- A team of Nutrition Evidence Systematic Review staff conducted a systematic review in collaboration with a group of experts called a Technical Expert Collaborative

What is the population of interest?

- Generally healthy infants and toddlers who were fed complementary foods and beverages from ages 0-24 months and had food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis examined through 18 years of age.

What evidence was found?

- This review includes 31 studies.
- These studies looked at the age when a complementary food or beverage was first introduced to the infant were first introduced and food allergy, atopic dermatitis/eczema, asthma, or allergic rhinitis.
- Complementary foods and beverages are foods and beverages other than human milk or infant formula provided to an infant or young child.
- Most evidence reported no relationship between age of complementary food

or beverage introduction and outcomes.

- There are limitations in the evidence as follows: use of less reliable methods to measure outcomes, only a few studies were done for some types of foods and/or outcomes, and other factors that may have had an impact on results were not always accounted for.

How up-to-date is this review?

This review includes literature from 1/1980 to 2/2017.

TECHNICAL ABSTRACT

Background

- Complementary feeding is the process that starts when human milk or infant formula is complemented by other foods and beverages, beginning during infancy and typically continuing to 24 months of age.
- This systematic review was conducted by a team of Nutrition Evidence Systematic Review (NESR) staff as part of the U.S. Department of Agriculture and Department of Health and Human Services Pregnancy and Birth to 24 Months Project.
- The goal of this systematic review was to answer the following research question: What is the relationship between timing of introduction of complementary foods/beverages and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis?

Conclusion Statement and Grades

- Moderate evidence suggests that there is no relationship between the age at which complementary feeding first begins and risk of developing food allergy, atopic dermatitis/eczema, or asthma during childhood. **Grade**: Moderate
- There is insufficient evidence to determine the relationship between the age at which complementary foods or beverages are first introduced and risk of developing allergic rhinitis during childhood. **Grade**: Grade Not Assignable

Methods

- This systematic review was conducted by a team of staff from NESR in collaboration with a Technical Expert Collaborative.
- A literature search was conducted using 4 databases (CINAHL, Cochrane, Embase, and PubMed) to identify articles published from January 1980 to February 2017 that examined the age when complementary foods and beverages (CFB) were first introduced and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis. CFB were defined as foods and beverages other than human milk or infant formula provided to an infant or young child. Outcomes included incidence and prevalence of food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis. A manual search was done to identify articles that may not have been included in the electronic databases searched. Articles were screened in a dual manner, independently by 2 NESR analysts, to determine which articles met predetermined criteria for inclusion.
- Data from each included article were extracted, risk of bias was assessed. The body of evidence was qualitatively synthesized, a conclusion statement was developed and the strength of the evidence (grade) was assessed using pre-established criteria including evaluation of the internal validity/risk of bias, adequacy, consistency, impact, and generalizability of available evidence. Research recommendations were identified.

Summary of Evidence

- Thirty-one observational studies are included in this systematic review, having examined the relationship between the age of first introduction to a CFB and risk of food allergies, atopic dermatitis/eczema, asthma, and allergic rhinitis occurring during childhood through 18 years of age.
    - The studies included in this review examined the timing of introduction to CFB, or the age at which infants were first introduced to any foods or beverages other than human milk or infant formula were first introduced to an infant. (Note: Studies that examined the timing of introduction of specific types of CFB, including common allergenic foods, such as peanuts, eggs, and fish, are addressed in a separate review).
    - These studies did not specify what food or beverage was first introduced. However, highly allergenic foods are not typically the first CFB introduced into an infant's diet; therefore, it is likely that the studies in this body of evidence reflect the first introduction of cereals, fruits, and vegetables.
    - Nine studies examined risk of food allergy, 20 studies examined risk of eczema or atopic dermatitis, eight studies examined risk of asthma, and four studies examined risk of allergic rhinitis.
- Most evidence reported no significant associations between age of CFB introduction and risk of food allergy. While some evidence suggested that earlier first introduction of CFB may be associated with increased risk of developing food allergy, confidence in the results was restricted by methodological limitations.
- The ability to draw stronger conclusions about the relationship between the timing of first introduction to CFB and the risk of atopic disease is due to several limitations:
    - Use of non-validated or unreliable measures to assess risk of atopic disease (e.g., parent report of a physician diagnosis or the child's symptoms), and assessment of outcomes later in childhood (through 10 years of age), when some atopic diseases, such as eczema, may have already resolved, or very early in childhood (3-4 months), before some atopic diseases may have occurred.
    - Lack of adjustment for key confounders such as consumption of human milk and/or human milk substitutes (e.g., cow's milk formula, hydrolyzed infant formula, or fluid cow's milk), parental smoking, and exposure to household pets
- Potential for reverse causality due to baseline atopic disease risk status impacting both the timing and types and amounts of CFB introduced, and risk of developing atopic disease.

FULL REVIEW

Systematic review question

What is the relationship between timing of introduction of complementary foods and beverages (CFB) food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis?

Conclusion statement

Moderate evidence suggests that there is no relationship between the age at which complementary feeding first begins and risk of developing food allergy, atopic dermatitis/eczema, or asthma during childhood.

There is insufficient evidence to determine the relationship between the age at which complementary foods or beverages are first introduced and risk of developing allergic rhinitis during childhood.

Grade

Moderate – Food allergy, atopic dermatitis/eczema, asthma; Grade Not Assignable – Allergic rhinitis

Summary

- Thirty-one observational studies are included in this systematic review, having examined the relationship between the age of first introduction to a CFB and risk of food allergies, atopic dermatitis/eczema, asthma, and allergic rhinitis occurring during childhood through 18 years of age.
    - The studies included in this review examined the timing of introduction to CFB, or the age at which infants were first introduced to any foods or beverages other than human milk or infant formula were first introduced to an infant. (Note: Studies that examined the timing of introduction of specific types of CFB, including common allergenic foods, such as peanuts, eggs, and fish, are addressed in a separate review[4]).
    - These studies did not specify what food or beverage was first introduced. However, highly allergenic foods are not typically the first CFB introduced into an infant's diet; therefore, it is likely that the studies in this body of evidence reflect the first introduction of cereals, fruits, and vegetables.
    - Nine studies examined risk of food allergy, 20 studies examined risk of eczema or atopic dermatitis, eight studies examined risk of asthma, and four studies examined risk of allergic rhinitis.
- Most evidence reported no significant associations between age of CFB

[4] Another systematic review examined the relationship between specific types and amounts of foods consumed during the complementary feeding period and risk of food allergies, atopic dermatitis/eczema, asthma, and allergic rhinitis. The timing of introduction of specific types of CFB (e.g., peanuts, eggs, fish) are addressed in that review.

introduction and risk of food allergy. While some evidence suggested that earlier first introduction of CFB may be associated with increased risk of developing food allergy, confidence in the results was restricted by methodological limitations.

- The ability to draw stronger conclusions about the relationship between the timing of first introduction to CFB and the risk of atopic disease is due to several limitations:
    - Use of non-validated or unreliable measures to assess risk of atopic disease (e.g., parent report of a physician diagnosis or the child's symptoms), and assessment of outcomes later in childhood (through 10 years of age), when some atopic diseases, such as eczema, may have already resolved, or very early in childhood (3-4 months), before some atopic diseases may have occurred.
    - Lack of adjustment for key confounders such as consumption of human milk and/or human milk substitutes (e.g., cow's milk formula, hydrolyzed infant formula, or fluid cow's milk), parental smoking, and exposure to household pets
- Potential for reverse causality due to baseline atopic disease risk status impacting both the timing and types and amounts of CFB introduced, and risk of developing atopic disease.

Description of the evidence

Thirty-one studies are included in the systematic review examining the relationship between timing of first introduction to any CFB and risk of one or more of the following: food allergy, atopic dermatitis, asthma, and allergic rhinitis occurring during childhood through 18 years (y) of age (**Table 1**). This table summarizes the results for each of the atopic diseases considered, and therefore, references may be repeated if they report results for two or more outcomes.

Timing of first CFB introduction was measured in a similar way across all studies, by determining the age at which a food or beverage other than human milk or infant formula was first introduced to the infant. These studies did not specify which specific CFB were introduced, but examined the age at which CF first began. However, since highly allergenic foods are not typically the first CFB introduced into an infant's diet in the US, it is likely that the studies in this body of evidence reflect the first introduction of cereals, fruits, and vegetables. Studies did differ in terms of whether timing was analyzed as a categorical or continuous variable, what categories of ages were evaluated, and the methods used for determining age of any CFB introduction. Most studies used introduction of any CFB before 3 or 4 mo as the earliest category, and after 6 mo as the latest category, though categories ranged from introducing CFB before 8 weeks (wk) to introduction between 7 and 12 mo of age.

The included studies examined risk of food allergy, atopic dermatitis, asthma, and allergic rhinitis, which were assessed at a range of ages, from infancy through 18 y of age, using varied diagnostic methods, as described below and in Table 1.

Summary of findings

Food allergy

Nine studies included in this systematic review examined the relationship between timing of first CFB introduction and risk of developing food allergy, including 7 prospective cohort studies (1-7) and 2 nested case-control studies (8, 9) (**Table 2**). Data from the following cohorts were examined in multiple studies: the Prevalence of Infant Food Allergy EuroPrevall (United Kingdom) study (8, 9), and an unnamed Finnish cohort (2, 3). Most studies either exclusively enrolled or enrolled a majority of subjects who were at high risk for developing atopic disease based on family history (parent or sibling) of atopic disease (1-3, 5-7). Both studies by Kajosaari et al. (2, 3) also exclusively enrolled breast fed (BF) infants, while the other studies included subjects who were BF, formula-fed (FF), or mixed-fed.

The studies used various methods and criteria for diagnosing food allergy, though most studies applied multiple valid and reliable methods, including food challenges, which are considered to be the best method for determining food allergy, as well as skin prick tests, Immunoglobulin E (IgE) levels, occurrence of symptoms post-ingestion, and/or elimination diets, and/or food challenges. However, a few studies relied on less valid methods, such as parent report of either symptoms or physician diagnosis to determine food allergy (3, 4). Risk of food allergy was determined at various ages, ranging from 6 mo through 6 y of age. Most studies adjusted for a number of key confounders, but a few made no adjustments for potential confounders (2, 3, 7).

Five studies reported no significant associations between the timing of any CFB introduction and risk of developing food allergy (1, 3-6). Most of these studies assessed risk of food allergy at 5-6 y of age. Four remaining studies reported that earlier introduction of CFB was associated with increased risk of food allergy. Grimshaw et al. (9) reported that CFB were introduced significantly earlier in food allergy cases compared with control infants (18 vs. 20 wk), and in categorical analyses, that later CFB introduction (≥17 vs. <17 wk) was significantly associated with reduced risk of food allergy at 2 y. Grimshaw et al. (8) analyzed the same data set, distinguishing between whether the food allergy was IgE-mediated or not, and found that earlier CFB introduction was significantly associated with non-IgE-mediated food allergy at 2 y, but not IgE-mediated food allergy. Kajosaari et al. (2) reported that earlier CFB introduction (3 vs. 6 mo) was significantly associated with increased risk of food allergy at 1 y. However, their subsequent publication (3) reported that this association was no longer significant when examining risk of food allergy at 5 y. Finally, Venter et al. (7) found that earlier CFB introduction (<16 vs. >16 wk) was associated with significantly decreased risk of food allergy at 1 y and 3 y. However, this study did not account for any potential confounders.

Atopic dermatitis

Twenty studies included in this systematic review examined the relationship between timing of CFB introduction and atopic dermatitis, including 19 prospective cohort studies (1-3, 6, 10-24) and 1 case-control study (25) (Table 2). Data from the following cohorts were examined in multiple studies, in which outcomes were

assessed in the same group of participants, but at different ages: the Lifestyle-Related Factors on the Immune System and the Development of Allergy in Childhood (Germany) study (23, 24), the German Infant Nutritional Intervention Program (12, 19), and an unnamed Finnish cohort (2, 3).

Half of the studies included a majority of subjects who were considered to be at high risk for atopic disease, having a family history (parent or sibling) of atopic disease (1-3, 6, 14, 16, 18, 20, 22-24), though most controlled for risk status in analyses (1, 6, 14, 16, 20, 23, 24). Kajosaari et al. (2, 3) also exclusively enrolled BF infants, while the other studies included subjects who were BF, FF, or mixed fed.

There was variability among studies in the methods and criteria used for diagnosing atopic dermatitis. Four studies based outcome assessment on a clinical exam done by study personnel (1, 3, 18, 19). However, most relied on less valid and/or reliable methods of parent report of symptoms or report of physician diagnosis. Age of outcome assessment occurred between 1 y and 6 y of age. Most studies adjusted for a number of key confounders, but several adjusted for only a few, or no potential confounders (2, 3, 11, 18, 22, 25).

Fifteen of the 20 studies reported no significant associations between timing of first CFB introduction and risk of developing atopic dermatitis (1, 3, 6, 10, 12, 14-19, 22-25).

The results from the studies that reported significant associations between timing of CFB introduction and risk of atopic dermatitis were mixed. Two studies found that earlier introduction of CFB was associated with increased risk of atopic dermatitis. Fergusson et al. (11) reported that earlier introduction of CFB (<4 vs. >4 mo) was significantly associated with increased risk of atopic dermatitis at 2 y. Kajosaari et al. (2) found that earlier CFB introduction (3 vs. 6 mo) was significantly associated with increased risk of atopic dematitis at 1 y. Two studies found that later introduction of CFB was significantly associated with increased risk of atopic dermatitis. Snijders et al. (20) found that later CFB introduction was significantly associated with increased risk of atopic dermatitis (3 vs 4-6 mo and 3 vs >7 mo) at 2 y. Taylor-Robinson et al. (21) found that later CFB introduction (>4 vs. <4 mo) was significantly associated with increased risk of atopic dermatitis at 5 y. Finally, Forsyth et al. (13) found that introducing CFB between 8-12 wk (vs. <8 or >12 wk) was significantly associated with greater incidence of atopic dermatitis between 53-104 wk.

In some of the studies that examined data from the same cohort, but measured outcomes at different ages, results were the same regardless of when the outcome was assessed (12, 19, 23, 24). However, 1 study reported that earlier CFB introduction was associated with increased risk of atopic dermatitis at 1 y (2), but this association was no longer significant at 5 y (3).

Asthma

Eight studies, including 7 prospective cohort studies and 1 case-control study, examined the relationship between timing of CFB introduction and asthma (3, 6, 16, 24, 26-29) (Table 2). Three of these studies exclusively enrolled subjects who were

at high risk for developing atopic disease, with all subjects having a family history (parent or sibling) of atopic disease (3, 6, 16). Kajosaari et al. (3) also exclusively enrolled BF infants, while the other studies included subjects who were BF, FF, or mixed-fed. The studies used similar methods and criteria for diagnosing asthma, relying primarily on parent report of symptoms, with only 2 studies using a physician to diagnose asthma (6, 28). Age of outcome assessment occurred between 2 y and 15 y, with most assessing outcomes between 4 y and 7 y of age. Most studies adjusted for a number of key confounders, but Kajosaari et al. (3) did not make any adjustments for potential confounders.

Seven of the 8 studies reported no significant associations between age of CFB introduction and asthma (3, 6, 16, 24, 26, 27, 29). In a case-control study conducted in Malaysia, Nathan et al. (28) found that children with asthma (ages 3-15 y) were significantly more likely to have had earlier introduction of CFB (<6 vs. >6 mo) than control children without asthma. However, this study had a number of limitations, including lack of control for several key confounders (education, SES, race/ethnicity, birth size), and use of non-validated, unreliable measures for assessing the timing of CFB introduction, which introduced the potential for recall bias, particularly among subjects recruited at older ages.

Allergic rhinitis

Four prospective cohort studies included in this review examined the relationship between timing of CFB introduction and allergic rhinitis (3, 6, 22, 24) (Table 2). Three of these studies exclusively enrolled subjects who were at high risk for developing atopic disease, with all subjects having a family history (parent or sibling) of atopic disease (3, 6, 22). Kajosaari et al. (3) enrolled exclusively BF infants, while the other studies included subjects who were BF, FF, or mixed-fed. As there are no standardized criteria for diagnosing allergic rhinitis, other than the presence of typical symptoms and corresponding positive skin prick tests, these studies are difficult to evaluate, as all relied on parent report of symptoms only. Age of outcome assessment occurred at 20 mo to 2 y (6, 22) or 5-6 y of age (3, 6, 24). Neither Kajosaari et al. (3) or Van Asperen et al. (22) adjusted for any potential confounders.

Most studies reported no significant associations between age of any CFB introduction and allergic rhinitis at 20 mo (22), 2 y (6), 5 y (6), or 6 y (24). Kajosaari et al. (3) reported that earlier introduction of solids (3 vs. 6 mo) was significantly associated with increased risk of allergic rhinitis at 5 y. However, allergic rhinitis was based on parent report of symptoms, and no adjustments were made for potential confounders.

Atopic disease

Three studies, including 2 prospective cohort studies (3, 30) and 1 case-control study (31), examined the relationship between timing of CFB introduction and atopic disease in general (Table 2). This category included studies that found 2 or more atopic diseases in the same subject. Two of these studies exclusively enrolled subjects who were at high risk for developing atopic disease, with all subjects having a family history (parent or sibling) of atopic disease (3, 30). Kajosaari et al.

(3) enrolled exclusively BF infants, while Poysa et al. (30) and Yung et al. (31) included subjects who were BF, FF, or mixed-fed. The studies varied in terms of the atopic diseases considered, diagnostic methods used, and ages when outcomes were assessed, with most relying on parent report of symptoms or a physician diagnosis. Finally, none of the studies adjusted for any potential key confounders.

All 3 studies reported no significant associations between age of CFB introduction and atopic disease, including atopic dermatitis, asthma, allergic rhinitis, and/or allergies (dust mite, food, drug, etc.) at 21 mo (31); atopic dermatitis, asthma, and/or positive skin prick test corresponding with history of food, pollen, or animal dander (birch, alm, timothy, mugwort, dog and cat epithelium, fish, milk, and wheat) at 5 y (3), or asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and/or food allergy at 9 y (30).

Evidence synthesis

Overall, moderate evidence suggests that there is no relationship between the age at which complementary feeding first begins and risk of developing food allergy, atopic dermatitis, or asthma during childhood. However, there is not enough evidence to determine whether there is a relationship with risk of developing allergic rhinitis.

Most of the evidence suggests no relationship between age of the first CFB introduction and risk of food allergy. While there is some evidence to suggest that earlier first introduction of CFB may be associated with increased risk of developing food allergy, confidence is limited by the use of the same cohort in multiple studies and concerns about the validity and reliability of methods used to assess food allergy. In addition, some studies did not account for one or more key confounders, or the specific types of CFB that were being introduced. Similarly, the preponderance of evidence suggests that there is no relationship between the age of first introduction to CFB and risk of developing atopic dermatitis and asthma. Finally, due to an inadequate number of studies with key methodological issues, it is not possible to draw conclusions about the relationship between age of CFB introduction and risk of developing allergic rhinitis.

There were several common methological limitations that could potentially lower the internal validity of the studies and reduce confidence in the findings. A number of studies used non-validated or unreliable measures (e.g., parent report of a child’s symptoms, or parent report of a physician diagnosis) to assess risk of atopic disease, particularly atopic dermatitis, asthma, and allergic rhinitis. In some cases, outcomes were assessed at inappropriate ages. For example, outcome assessment sometimes occurred later in childhood (through 10 years of age), when some atopic diseases, such as atopic dermatitis, may have already resolved, or very early in infancy (3-4 months), before atopic diseases may have emerged. In addition, there was a lack of adjustment for key confounders, such as infant milk feeding practices (e.g., human milk, cow’s milk formula, hydrolyzed infant formula, or fluid cow’s milk), parental smoking, exposure to household pets, and the types of CFB introduced.

Subjects in the studies are generalizable to the U.S. population. The studies were

conducted in a number of countries that were all determined to be “very high” or “high” according to the 2014 Human Development Index (HDI, 2014). Six studies were conducted in the United Kingdom, 5 each in Finland and Germany, 4 in the US, 3 in Australia, 2 in New Zealand, and 1 study each from Hong Kong, Malaysia, Mexico, Sweden, Taiwan, and the Netherlands.

However, because many of the studies included in this review exclusively enrolled or enrolled a majority of subjects who were at higher risk than the general population for developing allergy and/or atopic disease based on family history of atopic disease, the potential for reverse causality needs to be considered. Having a family background of atopic disease, such as 1 or both parents or a sibling with a diagnosed atopic disease, is 1 of the key risk factors for development of atopic diseases. In addition, known risk status could impact the timing, types, and amounts of CFB that were introduced, as well as risk of developing various atopic diseases in early childhood. However, despite the inclusion of higher risk populations in this body of evidence, the results are probably generalizable to infants and toddlers who are lower risk for atopic disease. In addition, most studies adjusted for atopy risk status in analyses.

Research recommendations

In order to better assess the relationship between CF and risk of atopic disease, additional research is needed that:

- Includes well-designed, targeted RCTs that address specific knowledge gaps
- Uses valid and reliable methods to assess infants’ dietary intake and established criteria, testing, and/or biomarkers to diagnose atopic disease at ages appropriate to the typical presentation of the disease
- Adjusts for key confounders, including infant milk feeding practices (e.g., human milk, cow’s milk formula, hydrolyzed infant formula, or fluid cow’s milk), parental smoking, exposure to household pets, and the types of CFB introduced
- Accounts for potential reverse causality by considering subjects’ baseline risk status for atopic disease
- Uses standard, consistent definitions of diet diversity, both in terms of the numbers and types of foods and food groups considered
- Considers the mechanisms by which specific types of foods, diet diversity, and dietary patterns may affect risk of developing atopic disease when determining which diet-health relationships to investigate, and what analyses are appropriate

Included articles

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Table 1. Description of studies examining the relationship between the timing of introduction of complementary foods and beverages (CFB) and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis.

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Chuang, 2011 Prospective Cohort Study; Taiwan (Taiwan Birth Cohort Study) Sample Size: Baseline N: 24200 Analytic N: 18733 Attrition: 23% Sample Size Calculation: NR Sex: 48% Female Race/Ethnicity: NR Atopic Disease Risk Status: 30% had parental allergic history; excluded children with doctor-diagnosed atopic dermatitis from 0-6mo Background Diet: 26.9% BF within 1mo	Intervention/Exposure: Age of CFB introduction: <4, 4-6, >6mo Assessment Methods: Maternal interview Outcomes: Atopic dermatitis Age: 18mo Assessment Methods: Atopic dermatitis: Maternal report of physician diagnosis	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Birth size; Gestational age; Smoking; Atopy risk status; Pets in home; Mold in home; Birth order; Parent age; Residence Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not account for high attrition Outcome assessors were not blinded Did not use valid/reliable methods for assessing outcomes (parent report) Did not adjust for key confounders (SES, race/ethnicity) Limited generalizability due to enrollment of population at high risk for atopic disease
Estrada-Reyes, 2007 Case-Control Study; Mexico Sample Size: Cases: 28 Controls: 28	Intervention/Exposure: Age of CFB introduction: <6, >6mo Assessment Methods: Maternal interview Outcomes: Atopic dermatitis	Confounders: The following confounders were accounted for: Atopy risk status Limitations: Cannot determine whether groups were similar at baseline on key characteristics

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Attrition: 0% Sample Size Calculation: NR Sex: 50% Female Race/Ethnicity: NR Atopic Disease Risk Status: 45% had family allergic history Background Diet: NR	Age: <3y Assessment Methods: Atopic dermatitis: Maternal report, confirmed by study personnel	Outcome assessors were not blinded Did not adjust for key confounders (education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking) Small sample size; study may have been underpowered
Fergusson, 1981 Prospective Cohort Study; New Zealand (Christchurch Health and Development Study) Sample Size: Baseline N: 1262 Analytic N: 1156 Attrition: 8% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 24% had parental atopy history Background Diet: EBF at 4mo: 19%	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Maternal interview, food diary Outcomes: Eczema Age: 2y Assessment Methods: Eczema: Maternal report; with some physician validation	Confounders: The following confounders were accounted for: Feeding practices; Atopy risk status Limitations: Cannot determine whether groups were similar at baseline on key characteristics Cannot determine recruitment methods, baseline characteristics, confounding factors, or blinding methods Outcome assessors were not blinded Did not adjust for key confounders (education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking) Limited generalizability due to lower rates of exclusive BF that may not be representative of current infant feeding practices
Fergusson, 1983 Prospective Cohort Study; New Zealand (Christchurch Health and Development Study)	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Maternal interview, food diary	Confounders: The following confounders were accounted for: Feeding practices; Atopy risk status

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Sample Size: Baseline N: 1265 Analytic N: 1110 Attrition: 12% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 11% had parental asthma history Background Diet: EBF at 4mo: 19%	Outcomes: Asthma Age: 4y Assessment Methods: Asthma: Maternal report of physician diagnosis, or history of wheezy bronchitis, with some physician validation	Limitations: Cannot determine whether groups were similar at baseline on key characteristics Cannot determine recruitment methods, baseline characteristics, confounding factors, or blinding methods Outcome assessors were not blinded Did not use valid/reliable measures to assess outcomes Did not adjust for key confounders (education, SES, sex, race/ethnicity, birth size, gestational age, smoking) Limited generalizability due to lower rates of exclusive BF that may not be representative of current infant feeding practices
Filipiak, 2007 Prospective Cohort Study; Germany (German Infant Nutritional Intervention Program) Sample Size: Baseline N: 5991 (N: 2252 in intervention group, N: 3739 in non-intervention group) Analytic N: 4753 Attrition: 21% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR	Intervention/Exposure: Age of CFB introduction: 1-4, 5-6, 7-12mo Assessment Methods: Parent questionnaire Outcomes: Eczema Age: 4y Assessment Methods: Eczema: Parent report of doctor diagnosis or recurrent symptoms lasting for 6mo up to 1y and 2wk at 2-4y	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Birth size; Gestational age; Smoking; Atopy risk status; Study region; siblings; pets) Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors (parent report) were not blinded Outcomes were not assessed using valid measures (parent report of physician diagnosis) Difficult to determine attrition rates based on sample sizes presented in text/tables

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Atopic Disease Risk Status: ~22% had familial history of eczema (40% in intervention group, 10% in non-intervention group); 100% of subjects in the intervention group had family history of atopic disease Background Diet: EBF at 4mo: 50%		Did not adjust for key confounders (SES, race/ethnicity, gestational age) Multi-component intervention may have confounded outcome (randomization to different formulas+ recommendations) Sample size calculations not reported.
Forsyth, 1993 Prospective Cohort Study; Scotland Sample Size: Baseline N: 671 Analytic N: 544 at 26wk, 548 at 52wk, 392 at 104wk Attrition: 19% at 26wk and 52wk, 50% at 104wk Sample Size Calculation: NR Sex: 52% Female Race/Ethnicity: NR Atopic Disease Risk Status: NR Background Diet: BF at 13wk: 14% EBF, 19.3% PBF, 66% MF	Intervention/Exposure: Age of CFB introduction: <8, 8-12, >12wk Assessment Methods: Maternal questionnaire Outcomes: Eczema Age: Asthma: 14-26wk Eczema: 53wk-104wk (~1-2y) Assessment Methods: Eczema: Parent report, medical record review; presence of itchy rash	Confounders: The following confounders were accounted for: SES; Sex; Feeding practices; Birth size; Smoking; Atopy risk status; Maternal age Limitations: Cannot determine whether groups were similar at baseline on key characteristics Cannot determine validity/reliability of measures used to assess outcomes High-attrition (50%) at 104wk not accounted for in analyses Did not adjust for key confounders (education, race/ethnicity, gestational age)
Grimshaw, 2013 Nested Case-Control Study; United Kingdom (Prevalence of Infant Food Allergy EuroPrevall) Sample Size:	Intervention/Exposure: Age of CFB introduction: Age in weeks, continuous Assessment Methods: Food diary Outcomes:	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Smoking; Atopy risk status; Pet ownership; Maternal Age; Single birth Limitations:

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Cases: 41 Controls: 82 Attrition: 0% Sample Size Calculation: NR Sex: 46% Female Race/Ethnicity: 95% Caucasian Atopic Disease Risk Status: 27% cases vs. 13% controls had maternal asthma; 54% vs. 38% had maternal allergy Background Diet: 94% initiated BF, 50% EBF at 9 weeks; Median BF duration 22wk, Median EBF duration 7 wk; CFB introduced at 20.3wk	Food allergy Age: 2y Assessment Methods: Food allergy: Parent report with clinical history, IgE≥0.35 and/or SPT wheal ≥3mm; exclusion diet with improved symptoms; and DBPCFC (including delayed reactions up to 48hr after the challenge)	Cannot determine whether participants were similar at baseline on key characteristics Did not adjust for key confounders (SES, race/ethnicity, birth size, gestational age) Small sample size; study may have been underpowered
Grimshaw, 2016 Nested Case-Control Study; United Kingdom (Prevalence of Infant Food Allergy EuroPrevall) Sample Size: Cases: 41 Controls: 82 Attrition: 0% Sample Size Calculation: NR Sex: 49 % Female Race/Ethnicity: 95% Caucasian Atopic Disease Risk Status: 67% had maternal atopy; 54% had paternal atopy; 22% had maternal food allergy; 12% had paternal food allergy	Intervention/Exposure: Age of CFB introduction: Age in weeks, continuous Assessment Methods: Food diary Outcomes: Food allergy (IgE and non-IgE mediated) Age: 2y Assessment Methods: Food allergy: Parent report with clinical history, IgE≥0.35 and/or SPT wheal ≥3mm; exclusion diet with improved symptoms; and DBPCFC (including delayed reactions up to 48hr after the challenge)	Confounders: The following confounders were accounted for: Gestational age; Atopy risk status; Child age; Dog at home; Received skin creams, powders, lotions; No nut/peanut intake during pregnancy; Reduced soy intake during BF Limitations: Cannot determine whether participants were similar at baseline on key characteristics Did not adjust for key confounders (SES, pets) Small sample size; study may have been underpowered

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Background Diet: 94% initiated BF, 50% EBF at 9 weeks; Median BF duration 22wk, Median EBF duration 7 wk; CFB introduced at 20.3wk		
Hesselmar, 2010 Prospective Cohort Study; Sweden (ALLERGY-FLORA) Sample Size: Baseline N: 207 Analytic N: 184 Attrition: 11% Sample Size Calculation: NR Sex: 50% Female Race/Ethnicity: NR Atopic Disease Risk Status: 80% had both parents, 49% maternal, 41% paternal history of asthma, AR, or eczema Background Diet: 88% BF; 76% still PBF at 6mo; Formula introduced ~5mo; median duration EBF 4mo, PB 7.5mo; Age introduced to solids (potatoes, root/vegetables, meats) 4mo; fruit 5mo; fish 10mo; hen's egg 12mo	Intervention/Exposure: Age of CFB introduction: Age in months, continuous (CFB: potatoes, root vegetables, vegetables, and meat) Assessment Methods: Food diary Outcomes: Food allergy, eczema, asthma Age: 18mo Assessment Methods: Food allergy: Symptoms (immediate or late-onset reaction) after food ingestion, with OFC, and/or food-specific IgE, SPT wheal ≥3mm, and/or GI biopsy/multi-organ reactions Eczema: Clinical exam	Confounders: The following confounders were accounted for: Sex; Feeding practices; Gestational age; Atopy risk status Limitations: Cannot determine whether participants were similar at baseline on key characteristics of race/ethnicity, SES, education, birth size/weight, or smoking exposure Cannot determine whether outcome assessors were blinded Did not adjust for key confounders (education, SES, race/ethnicity, birth size, smoking) CFB included only “non allergenic” foods; allergenic foods examined seperately
Hetzner, 2009 Prospective Cohort Study; United States (Early Child Longitudinal Study-Birth Cohort) Sample Size:	Intervention/Exposure: Age of CFB introduction: <6, >6mo Assessment Methods: Maternal interview Outcomes:	Confounders: The following confounders were accounted for: Education; SES; Sex; Race/ethnicity; Feeding practices; Birth size; Smoking Limitations:

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Baseline N: 10700 Analytic N: 7900 Attrition: 26% Sample Size Calculation: NR Sex: 49% Female Race/Ethnicity: 54% White-Non Hispanic; 13% Black-African American-Non Hispanic; 26% Hispanic; 3% Asian Atopic Disease Risk Status: NR Background Diet: 70% initiated BF; 78% introduced formula<6mo; 74% introduced to CFB<6mo; 15% introduced finger-foods <6mo	Asthma Age: 2y Assessment Methods: Asthma: Maternal report	Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Outcome measures used were not valid/reliable (maternal report of asthma with no criteria or definition provided, and at an arly age when asthma diagnoses are less reliable) Did not adjust for key confounders (gestational age, atopy risk status)
Illi, 2004 Prospective Cohort Study; German (German Multicenter Atopy Study) Sample Size: Baseline N: 1314 Analytic N: 858 Attrition: 35% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 73% had parental atopy history Background Diet:	Intervention/Exposure: Age of CFB introduction: Quartiles (not described) Assessment Methods: Parent interview Outcomes: Atopic dermatitis Age: 2y Assessment Methods: Atopic dermatitis: Parent report of physician diagnosis or symptoms; or visible atopic dermatitis at follow-up	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Smoking; Atopy risk status; Pets; older siblings; # of infectious diseases Limitations: Cannot determine whether participants were similar at baseline on key characteristics of SES, race/ethnicity, birth size, or gestational age Outcome assessors were not blinded Outcome measures used were not valid/reliable Did not adjust for key confounders (SES, race/ethnicity, birth size, gestational age) Did not describe categories (quartiles) anlyzed for age of CFB introduction; did not show data for analyses wih risk of AD, and did not report whether analyses were

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
92% initiated BF; 49% received supplements in first days of life (36% of which was cow's milk formula, often partially hydrolyzed) 53% introduced CFB <3mo; atopic parents introduced CFB later than non-atopic parents		done for other outcomes reported in the study (food allergen sensitization, asthma, wheeze)
Joseph, 2011 Prospective Cohort Study; United States (Wayne County Health, Environment, Allergy and Asthma Longitudinal (WHEALS) Study) Sample Size: Baseline N: 1258 Analytic N: 594 Attrition: 53% Sample Size Calculation: NR Sex: NR Race/Ethnicity: 61% Black Atopic Disease Risk Status: 45% had parental history of atopy Background Diet: 77% ever BF; 73% BF <6mo; 40% introduced to CFB <4mo	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Parent interview Outcomes: Atopic dermatitis Age: 2-3y Assessment Methods: Atopic dermatitis: NR	Confounders: The following confounders were accounted for: Education; SES; Sex; Race/ethnicity; Feeding practices; Smoking; Atopy risk status; Birth order; Marital status Limitations: Cannot determine whether participants were similar at baseline on key characteristics of gestational age or birth weight Cannot determine whether outcome assessors were blinded Validity/Reliability of measures used not clear Did not adjust for key confounders (birth size, gestational age) Asthma defined as early childhood wheezing
Kajosaari, 1983 Prospective Cohort Study; Finland Sample Size: Baseline N: 135	Intervention/Exposure: Age of CFB introduction: ~3, 6mo Assessment Methods: NR Outcomes:	Confounders: No confounders were adjusted for Limitations: Outcome assessors were not blinded

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Analytic N: 135 Attrition: N/A Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 100% had familial risk (either parent either asthma or allergy) Background Diet: EBF to 6mo: 52%; no infants received formula Age of CFB introduction: 48% by 3mo	Food allergy, eczema Age: 1y Assessment Methods: Food allergy: History of skin rash or vomiting after ingestion, confirmed by elimination diet and home challenges Eczema: Parent report of physician diagnosis of eczema, and/or diagnosis by study personnel	Cannot determine whether participants were similar on any baseline characteristics Did not adjust for key confounders (education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking, atopy risk status) Did not use valid/reliable measures for outcome measure for food allergy Limited generalizability due to exclusive enrollment of high risk infants
Kajosaari, 1994 Prospective Cohort Study; Finland Sample Size: Baseline N: 135 Analytic N: 135 Attrition: N/A Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 100% had familial risk (either parent either asthma or allergy) Background Diet: EBF to 6mo: 52%; no infants received formula Age of CFB introduction: 48% by 3mo	Intervention/Exposure: Age of CFB introduction: ~3, 6mo Assessment Methods: NR Outcomes: Food allergy, atopic eczema, asthma, allergic rhinitis, atopic disease Age: 5y Assessment Methods: Food allergy: Parent report of repeated skin rash, urticaria or heavy vomiting after ingestion Atopic eczema: Examination by study personnel Asthma: Parent reported asthma diagnosis Allergic rhinitis: History of seasonal symptoms (nasal discharge, itching conjunctivities, wheezing)	Confounders: No confounders were adjusted for Limitations: Outcome assessors were not blinded Cannot determine whether participants were similar on any baseline characteristics Did not adjust for key confounders (education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking, atopy risk status) Did not use valid/reliable measures to assess outcomes, especially food allergy Limited generalizability due to exclusive enrollment of high risk infants Small sample size; study may have been underpowered

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
	during pollen season or associated with animal contacts Atopic disease: Atopic eczema, asthma, or positive SPT corresponding with history of food, pollen, or animal dander (birth, alm, timothy, mugwort dog & cat epithelium, fish, milk, & wheat	
Luccioli, 2014 Prospective Cohort Study; United States (Infant Feeding Practices Study II Year 6 Follow-Up Study) Sample Size: Baseline N: 1531 Analytic N: 1363 Attrition: 12% Sample Size Calculation: NR Sex: 51% Female Race/Ethnicity: 86% White Non-Hispanic; 2% Asian Non-Hispanic; 4% Black Non-Hispanic; 6% Hispanic; 2% Other Atopic Disease Risk Status: 23% had parent history of food allergy; 44% had parent history of atopy Background Diet: 43% EBF at 0mo, 30% at 1-3mo, 27% at 4mo+; Introduced to CFB: 34% at 1-3mo; 40% at 4-5mo; 17% at 6-12mo; 9% NR	Intervention/Exposure: Age of CFB introduction: 1-3/<4, 4-5, 6-12mo, NR Assessment Methods: Maternal questionnaire Outcomes: Food allergy Age: 6y Assessment Methods: Food allergy: Maternal report of physician diagnosis	Confounders: The following confounders were accounted for: Education; SES; Sex; Race/ethnicity; Feeding practices; Smoking; Atopy risk status; Delivery mode; Parity Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Outcome measures used were not valid/reliable Did not adjust for key confounders (birth size, gestational age)
McGowan, 2015 Prospective Cohort Study; United States	Intervention/Exposure: Age of CFB introduction: Age in wk, continuous	Confounders:

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
(Urban Environment and Childhood Asthma) (URECA) Sample Size: Baseline N: 609 Analytic N: 516 Attrition: 15% Sample Size Calculation: NR Sex: 56% Female Race/Ethnicity: 61% Black, 16% Hispanic, 7% Other Atopic Disease Risk Status: 80% had parental history of allergic rhinitis, eczema, or asthma Background Diet: 44% ever BF, 18% BF at 3mo; CFB introduced at 15wk (SD=~8.5wk)	Assessment Methods: Maternal interview Outcomes: Food allergy Age: 5y Assessment Methods: Food allergy: Positive IgE level (>0.35 kU/L) to milk, egg, and/or peanut, avoidance of sensitized foods, and clinical confirmation (parent report of previous food reaction to milk, egg or peanut; or classified as FA by allergist consult)	The following confounders were accounted for: Sex; Gestational age; Atopy risk status; Site Limitations: Cannot determine whether groups were similar at baseline on key characteristics Limited information provided about CFB assessment Did not use valid/reliable measures to diagnose food allergy Cannot determine whether outcome assessors were blinded Did not adjust for key confounders (education, SES, race/ ethnicity, feeding practices, birth size, smoking) Generalizability limited to inner-city children in small number of US cities with parental history of allergy/asthma Large number of subjects classified as "possibly allergic" and weren't included in analyses
Mihrshahi, 2007 Prospective Cohort Study; Australia (Childhood Asthma Prevention Study) Sample Size: Baseline N: 616 Analytic N: 516 Attrition: 16% Sample Size Calculation: NR	Intervention/Exposure: Age of CFB introduction: <3, >3mo Assessment Methods: Maternal interview Outcomes: Eczema, asthma Age: 5y Assessment Methods:	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Birth size; Gestational age; Smoking; Atopy risk status; Intervention group Limitations: Cannot determine whether groups were similar at baseline on key characteristics

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 100% had one or more parents or siblings had asthma or wheezing Background Diet: 90% ever BF, 34% EBF at 3mo, 2% EBF at 6mo; CFB introduced by 26% at 3mo	Eczema: Presence of flexural eczema, or a history of itchy rash coming and going for >3mo, and at least one of the following: seeking medical care for diagnosed eczema/atopic dermatitis or using steroid or emollient creams in the last 12mo Asthma (probable current): Any wheeze in last 12mo in children who either had asthma diagnosed by a doctor or at a hospital, or a positive bronchodilator test	Did not use valid/reliable measures to assess all outcomes (asthma) Did not adjust for key confounders (SES, race/ethnicity) Generalizability limited to those with a family history of asthma
Nathan, 2012 Case-Control Study; Malaysia Sample Size: Asthma Cases: 78 Controls: 78 Attrition: NA Sample Size Calculation: NR Sex: 46% Female Race/Ethnicity: 65% Malay, 13% Chinese, 22% Indian Atopic Disease Risk Status: 77% cases vs 21% controls had family history of atopy, 80% vs 21% had family history of asthma Background Diet: 28% were EBF >6mo	Intervention/Exposure: Age of CFB introduction: <6, >6mo Assessment Methods: Parent questionnaire Outcomes: Asthma Age: 3-15y Assessment Methods: Asthma: Recurrent episodes of doctor-diagnosed wheezing with use of acute reliever and/or inhaler medication	Confounders: The following confounders were accounted for: Sex; Feeding practices; Gestational age; Smoking; Atopy risk status; Mode of delivery Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not use valid/reliable measures, particularly for assessing timing of CFB introduction Cannot determine whether length of follow-up was similar between groups Did not adjust for key confounders (Education, SES, race/ethnicity, birth size) Potential for recall bias, particularly among subjects recruited at older ages Study may have been underpowered
O'Donovan, 2016 Prospective Cohort Study; United Kingdom (Cork BASELINE Study)	Intervention/Exposure: Age of CFB introduction: <17, >26wk Assessment Methods: Maternal interview	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Birth size; Smoking; Atopy risk status; Domestic pet, body composition, cord

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Sample Size: Baseline N: 1,537 Analytic N: 709 Attrition: 54% Sample Size Calculation: NR Sex: 48% Female Race/Ethnicity: NR Atopic Disease Risk Status: 43% had maternal family history or atopy, 34% had parental family history of atopy Background Diet: 14% EBF at 2mo; 22% BF at 6mo; 19% introduced to CFB by 17wk, 6% introduced >26wk	Outcomes: Atopic dermatitis Age: 12mo Assessment Methods: Atopic dermatitis: Parent report, with formal diagnosis using UK Working Party Diagnostic Criteria	vitamin D status, season of birth, rural/urban, maternal alcohol and vit D intake at 15wk, C-section, marital status, maternal BMI, maternal age Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not adjust for key confounders (SES, race/ethnicity, gestational age) Did not assess the impact of high loss to follow-up (>50% by 12mo)
Poysa, 1989 Prospective Cohort Study; Finland Sample Size: Baseline N: 100 Analytic N: 70 Attrition: 30% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: All subjects had family atopy history	Intervention/Exposure: Age of CFB introduction: <3, 3-6, >6mo (CFB: avoided “classic dietary allergens” until 9mo) Assessment Methods: Parent questionnaire Outcomes: Atopic dermatitis Age: 5y Assessment Methods: Atopic dermatitis: Diagnosis by a dermatologist; pruritic dermatitis accompanied by dry skin on the face in infancy and on flexural surfaces of the extremities later	Confounders: No confounders were adjusted for Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not adjust for key confounders (SES, sex, education, race/ethnicity, birth size, gestational age, feeding practices, atopy risk status, smoking) Did not account for high loss to follow-up (~30%) Did not report statistical results of analyses Limited generalizability due to exclusive enrollment of high risk infants

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Background Diet: Subjects with atopy history advised to BF for >3mo, to not introduce formula or cow's milk before 3mo, and to avoid the "classic dietary allergens until 9mo; 52% followed this diet BF: 24% <3mo, 14% 3-6mo, 61% >6mo; FF: 36% <3mo, 30% 3-6mo, 44% >6mo; CFB: 23% <3mo, 73% 3-6mo, 4% >6mo		
Poysa, 1991 Prospective Cohort Study; Finland Sample Size: Baseline N: 100 Analytic N: 68 Attrition: 32% Sample Size Calculation: NR Sex: NR Race/Ethnicity: NR Atopic Disease Risk Status: 100% had family history of atopy Background Diet: Subjects with atopy history advised to BF for >3mo, to not introduce formula or cow's milk before 3mo, and to avoid the "classic dietary allergens until 9mo; 52% followed this diet BF: 24% <3mo, 14% 3-6mo, 61% >6mo; FF: 36% <3mo, 30% 3-6mo, 44% >6mo; CFB: 23% <3mo, 73% 3-6mo, 4% >6mo	Intervention/Exposure: Age of CFB introduction: <3, 3-6, >6mo Assessment Methods: Parental questionnaire Outcomes: Atopy Age: 9y Assessment Methods: Atopy: Parent report of physician diagnosis of asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis (diagnosis made by dermatologist), and/or food allergy; allergies to fruit and or apple tested at home (elimination diet) and allergies to eggs or fish confirmed by hospital challenge)	Confounders: No confounders were adjusted for Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not account for high loss to follow-up (~30%) Did not use valid/reliable measures to measure outcomes Did not adjust for key confounders (SES, sex, education, race/ethnicity, birth size, gestational age, feeding practices, atopy risk status, smoking)
Sandini, 2011 Prospective Cohort Study; Finland	Intervention/Exposure: Age of CFB introduction: <4, >4mo	Confounders:

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Sample Size: Baseline N: 1223 Analytic N: 925 at 2y, 891 at 5y Attrition: 24% at 2y, 27% at 5y Sample Size Calculation: Yes, but based on RCT of probiotics for allergy prevention conducted in this same population Sex: 50% Female Race/Ethnicity: NR Atopic Disease Risk Status: 100% had at least one parent with an allergic disease Background Diet: 45% EBF for 2-4mo, 61% BF >6mo, solids started at ~4mo (SD=0.7), with 67% ≥4mo	Assessment Methods: Parent questionnaire Outcomes: Food allergy, eczema, asthma, allergic rhinitis Age: 2y, 5y Assessment Methods: Food allergy: OFC in infants whose food-related symptoms (urticaria, eczema, vomiting, loose stools, abdominal pain, and excessive crying) improved during a 2wk elimination diet Eczema: Itchy skin plus all or 3 of the following: history of atopic disease in the family, dry skin during the last year, history of eczema, or visible eczema involving typical sites Asthma: 2+ physician-diagnosed wheezing episodes with persistent cough or as exercise-induced (including giggling and crying) symptoms; verified by the study pediatrician review of patient records Allergic rhinitis: Allergen-specific sensitization with a history of 2 or more symptoms (nasal discharge, blockage, or sneezing/itching) recurrently during antigen contact	The following confounders were accounted for: Sex; Feeding practices; Gestational age; Smoking; Atopy risk status; Delivery mode, siblings, antibiotic use, airway infections, dog/cat exposure; RCT study group Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not adjust for key confounders (SES, race/ethnicity, birth size) Outcome assessors were not blinded Did not define age of CFB introduction Limited generalizability due to exclusive enrollment of high risk infants
Schoetzau, 2002 Prospective Cohort Study; Germany(German Infant Nutritional Intervention Program) Sample Size: Baseline N: 2252	Intervention/Exposure: Age of CFB introduction: 1-16, 17-24, >24wk Assessment Methods: Food diary Outcomes:	Confounders: The following confounders were accounted for: Education; Sex; Race/ethnicity; Feeding practices; Gestational age; Smoking; Atopy risk status; Pets Limitations:

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Analytic N: 1121 Attrition: 50% Sample Size Calculation: NR Sex: 49% Female Race/Ethnicity: NR Atopic Disease Risk Status: 42% had 1+ core family members with atopic dermatitis; all infants had extended family members with some atopic disease Background Diet: 23% formula fed, 77% BF	Atopic dermatitis Age: 1y Assessment Methods: Atopic dermatitis: Physician diagnosis defined by a combination of diagnostic criteria, including typical morphology and distribution of skin lesions (face, neck and scalp, flexural folds, hands and extensor sides of extremities); pruritus (signs of scratching); and a tendency towards chronicity (duration of least 14d and/or relapsing)	Cannot determine whether groups were similar at baseline on key characteristics Did not account for high loss to follow-up (>50% by 1y) Did not adjust for key confounders (SES, birth size)
Snijders, 2008 Prospective Cohort Study; The Netherlands (KOALA Birth Cohort Study) Sample Size: Baseline N: 2834 Analytic N: 2558 Attrition: 10% Sample Size Calculation: NR Sex: 49% Female Race/Ethnicity: NR Atopic Disease Risk Status: 60% had parental allergic disease, 19% had sibling allergic disease Background Diet: 15% never BF, 33% BF 0-3mo, 17% BF 4-6mo, 15% BF 7-9mo, 17% BF >9mo; 39% introduced to cow milk products by 3mo; 89% introduced to other solid foods from 4-6mo	Intervention/Exposure: Age of CFB introduction: <3, 4-6, >7mo Assessment Methods: Parent questionnaire Outcomes: Eczema/atopic dermatitis Age: 2y Assessment Methods: Eczema: Parent report of itchy rash Atopic dermatitis: Parent report of the presence of itchy rash, history of flexural dermatitis,, presence of visible flexural dermatitis, and onset before 2y; UK AD scoring system with home visit and visualization of skin at 2y)	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Smoking; Atopy risk status; Conventional/ alternative lifestyle; Maternal age at delivery Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not use valid/reliable measures (parent reported outcomes) Did not adjust for key confounders (SES, race/ethnicity, birth size, gestational age)

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Taylor-Robinson, 2016 Prospective Cohort Study; United Kingdom (UK Millennium Cohort Study) Sample Size: Baseline N: 14499 Analytic N: 11537 Attrition: 20% Sample Size Calculation: NR Sex: 49% Female Race/Ethnicity: 88% White, 3% Mixed, 2% Indian, 4% Pakistani/ Bangladeshi, 3% Black Atopic Disease Risk Status: 23% of mothers had asthma or eczema Background Diet: 31% never BF, 27% BF >6mo; 55% introduced to cow's milk <9mo	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Parent questionnaire (ISAAC) Outcomes: Eczema Age: 5y Assessment Methods: Eczema: Parent report of whether their child had 'ever had eczema'	Confounders: The following confounders were accounted for: Education; Sex; Race/ethnicity; Feeding practices; Birth size; Gestational age; Smoking; Atopy risk status; Maternal age, maternal BMI, C-section, antibiotic use, dampness at home, exposure to pollution and "grime", furry pets, siblings Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not use valid/reliable measures (parent reported outcomes) Did not adjust for key confounders (SES)
Van Asperen, 1984 Prospective Cohort Study; Australia Sample Size: Baseline N: NR Analytic N: 79 Attrition: Cannot determine Sample Size Calculation: NR Sex: NR	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Parent interview Outcomes: Atopic dermatitis, allergic rhinitis Age: 20mo Assessment Methods: Atopic dermatitis: Parent report of evidence of areas of scaly, erythematous, pruritic dermatitis primarily	Confounders: No confounders were adjusted for Limitations: Cannot determine whether groups were similar at baseline on key characteristics Cannot determine whether outcome assessors were blinded Did not use valid/reliable measures (to assess outcomes)

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Race/Ethnicity: NR Atopic Disease Risk Status: 100% had family history (parent or sibling) of atopic disease Background Diet: 25% EBF at 4mo	involving flexural folds, face, cheeks or areas behind the ears but excluding xeroderma alone Allergic rhinitis: Parent report of history of nasal discharge and/or blockage occurring continuously for at least 4wk and excluding obvious infective rhinitis	Did not adjust for any key confounders (Education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking, atopy risk status) Limited generalizability due to exclusive enrollment of high risk subjects Small sample size; study may have been underpowered
Venter, 2009 Prospective Cohort Study; United Kingdom Sample Size: Baseline N: 969 Analytic N: 927 at 3mo, 913 at 6mo, 900 at 9 and 12mo, 858 at 24mo Attrition: 4% at 3mo, 6% at 6mo, 7% at 9 and 12mo, 12% at 24mo Sample Size Calculation: NR Sex: 48% Female Race/Ethnicity: NR Atopic Disease Risk Status: 83% had family history of allergic disease Background Diet: BF duration: 42d, formula introduced ~14d; 27% introduced CFB <3mo, 82% <4mo, 100% by 6mo	Intervention/Exposure: Age of CFB introduction: <4, >4mo Assessment Methods: Parental questionnaire Outcomes: Food allergy Age: 1y, 3y Assessment Methods: Food allergy: Parent report of symptoms, SPT wheal >3mm (milk, egg, wheat, cod, peanut, sesame), and DBPCFC	Confounders: No confounders were adjusted for Limitations: Cannot determine whether groups were similar at baseline on key characteristics Cannot determine whether outcome assessors were blinded Did not adjust for any key confounders (Education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking, atopy risk status)Small number of subjects diagnosed with food allergy; study may have been underpowered
Wilson, 1998 Prospective Cohort Study; Australia	Intervention/Exposure: Age of CFB introduction: <15, >15wk	Confounders: The following confounders were accounted for: SES; Sex; Feeding practices; Birth size; Gestational age;

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Sample Size: Baseline N: 674 Analytic N: 545 Attrition: 19% Sample Size Calculation: NR Sex: 54% Female Race/Ethnicity: NR Atopic Disease Risk Status: 25% had paternal history of allergic disease, 27% had maternal history of allergic disease Background Diet: 26% EBF at 15wk, 37% partial BF at 15wk, 37% formula fed at 15wk; 73% introduced to CFB <15wk	Assessment Methods: Parent questionnaire Outcomes: Asthma Age: ~7.3y (6.1-9.9y) Assessment Methods: Asthma: Parent report of doctor diagnosis at any time since birth (ever) or if the child was currently receiving asthma treatment (current)	Smoking; Atopy risk status; Weight at first solid feed; Maternal height; Maternal blood pressure; Parity Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not use valid/reliable measures (to assess outcomes) Did not adjust for any key confounders (Education, race/ethnicity)
Yung, 2015 Case-Control Study; China (Hong Kong) Sample Size: Cases: 71 Controls: 135 Attrition: NA Sample Size Calculation: NR Sex: 46% Female Race/Ethnicity: NR Atopic Disease Risk Status: 44% had parental history of atopic disease	Intervention/Exposure: Age of CFB introduction: Age in wks, continuous Assessment Methods: Maternal questionnaire Outcomes: Atopic disease Age: ~21mo (SD: 11mo) (range: 4mo-3y) Assessment Methods: Atopy: Physician-diagnosed atopy (eczema or allergic dermatitis, asthma, rhinitis, conjunctivitis (not related to infection), and allergies (dust mite, food, drug, etc.); diagnostic methods and criteria not described	Confounders: No confounders were adjusted for Limitations: Cannot determine whether groups were similar at baseline on key characteristics Did not adjust for any key confounders (Education, SES, sex, race/ethnicity, feeding practices, birth size, gestational age, smoking, atopy risk status) Cannot determine whether valid/reliable measures were used to assess outcomes

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Background Diet: 75% EBF at birth, 64% EBF at 3mo, 27% EBF at 6mo; age when solid food was introduced ~25wk		Retrospective nature of dietary recall to determine age of introduction to solid foodsSmall sample size; study may have been underpowered
Zutavern, 2006 Prospective Cohort Study; Germany (Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood) Sample Size: Baseline N: 3097 Analytic N: 2612 Attrition: 16% Sample Size Calculation: NR Sex: 48% Female Race/Ethnicity: NR Atopic Disease Risk Status: 53% with parental history of atopy Background Diet: 59% EBF 4 mo, 35.7% mixed fed, 5.2 % formula fed	Intervention/Exposure: Age of CFB introduction: 0-4, 5-6, >6mo Assessment Methods: Parent questionnaire Outcomes: Atopic dermatitis Age: 2y Assessment Methods: Doctor-diagnosed atopic dermatitis: Parent report of physician diagnosis of AD in the last 6mo Symptomatic atopic dermatitis: Parent report of itching eczema within the last 6mo that was either recurrent or lasted for 2wk and that affected the skin creases, face, neck, extremities, hands, feet, or trunk (not underneath the diaper) Early skin or allergic symptoms: Parent affirmative response to, “Has a doctor diagnosed your child with 1 of the following conditions within the first 6mo of life: atopic dermatitis; allergic or atopic eczema; food allergy, hives, urticaria, or allergic edema; milk crust or seborrheic eczema; eczema without further specification?” or when parents reported an increase of eczema as a result of food intolerance within the first 6mo of their child’s life	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Birth size; Smoking; Atopy risk status; Study center; Number of siblings Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not use valid/reliable measures to assess outcomes (parent report) Did not adjust for any key confounders (SES, race/ethnicity, gestational age, pets)
Zutavern, 2008	Intervention/Exposure: Age of CFB introduction: <4, 4-6, >6mo	Confounders: The following confounders were accounted for: Education; Sex; Feeding practices; Smoking; Atopy risk

References; Subject Characteristics (Sample Size, Sex, Race/Ethnicity, Atopic Disease Risk Status; Background Diet)	Independent Variable/Exposure, Outcomes	Confounders, Limitations
Prospective Cohort Study; Germany (Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood) Sample Size: Baseline N: 3097 Analytic N: 2073 Attrition: 33% Sample Size Calculation: NR Sex: 49% Female Race/Ethnicity: NR Atopic Disease Risk Status: 53% with parental history of atopy Background Diet: 59% EBF at 4mo, 35.7% mixed fed, 5.2% formula fed	Assessment Methods: Parent questionnaire Outcomes: Eczema, asthma, allergic rhinitis Age: 6y Assessment Methods: Atopic dermatitis: Parent report of physician diagnosis , or itching eczema within the last 6mo that was either recurrent or lasted for 2wk and that affected the skin creases, face, neck, extremities, hands, feet, or trunk (not underneath the diaper) Asthma: Parent report of physician diagnosis of asthma or report of wheezing or intake of asthma medication Allergic rhinitis: Parent report of physician diagnosis of allergic rhinitis, or report of sneezing or a blocked or running nose without having a cold	status; Study center, number of siblings; Maternal age at birth Limitations: Cannot determine whether groups were similar at baseline on key characteristics Outcome assessors were not blinded Did not use valid/reliable measures to assess outcomes (parent report) Did not adjust for any key confounders (SES, race/ethnicity, gestational age, birth size, pets)

Table 2. Results from studies that examined the relationship between age of first introduction of any complementary foods and/or beverages (CFB) and food allergy, atopic dermatitis, asthma, and allergic rhinitis.

Reference[1]; Study design; Country; Sample size	Age of CFB introduction	Results
FOOD ALLERGY		
Grimshaw, 2013 (9); Nested Case-Control Study (Prevalence of Infant Food Allergy EuroPrevall); United Kingdom; Food Allergy Cases: 41, Controls: 82	Age in weeks, mean	Food allergy cases vs. controls: 18wk vs 20wk; P=0.044
	>17wk vs. <17wk	Food allergy at 2y: OR=0.245; 95% CI: 0.088, 0.679; P<0.05
Grimshaw, 2015 (8); Nested Case-Control Study (Prevalence of Infant Food Allergy EuroPrevall); United Kingdom; Food Allergy Cases: 41, Controls: 82	Age in weeks, cases vs. controls	Food allergy at 2y: OR=0.506, 95% CI: 0.282, 0.908; P=0.022
		Food allergy, non-IgE-mediated at 2y: OR=0.60, 95% CI: 0.40, 0.89; P=0.011
		Food allergy, IgE-mediated, at 2y: No significant associations
Hesselmar, 2010 (1); Prospective Cohort Study (ALLERGY-FLORA); Sweden; N: 184	Age in months, continuous	Food allergy at 18mo: No significant associations
Kajosaari, 1983 (2); Prospective Cohort Study; Finland; N: 135	~3 vs. 6mo	Food allergy at 1y: 37% vs.7%; P<0.001
Kajosaari, 1994 (3); Prospective Cohort Study; Finland; N: 135	~3 vs. 6mo	Food allergy at 5y: No significant associations
Luccioli, 2014 (4); Prospective Cohort Study; United States (Infant Feeding Practices Study II Year 6 Follow-Up Study); N: 1363	1-3/<4 vs. 4-5 vs. 6-12mo	Food allergy at 6y: No significant associations
McGowan, 2015 (5); Prospective Cohort Study (Urban Environment and Childhood Asthma Cohort); United States; N: 516	Categories not defined	Food allergy at 5y: No significant associations
Sandini, 2011 (6); Prospective Cohort Study; Finland; N: 925 at 2y, 891 at 5y	Categories not defined	Food allergy at 2y and 5y: No significant associations

Reference[1]; Study design; Country; Sample size	Age of CFB introduction	Results
Venter, 2009 (7); Prospective Cohort Study; United Kingdom; N: 927 at 3mo, 913 at 6mo, 900 at 9 and 12mo, 858 at 24mo	<4 vs. >4mo	Food allergy at 1y: OR=0.41, 95% CI 0.18, 0.89; P=0.02 Food allergy at 3y: OR=0.51, 95% CI: 0.28, 0.92; P=0.02
ATOPIC DERMATITIS		
Chuang, 2011 (10); Prospective Cohort Study; Taiwan; N: 18733	<4, 4-6, >6mo	Atopic dermatitis at 18mo: No significant associations
Estrada-Reyes, 2007 (25); Case-Control Study; Mexico; Atopic Dermatitis Cases: 28; Controls: 28	<6, >6mo	Atopic dermatitis, cases vs. controls: No significant associations
Fergusson, 1981 (11); Prospective Cohort Study; New Zealand; N: 1156	<4, >4mo	Atopic dermatitis at 2y: 17.78% vs. 12.58%; P<0.05
Filipiak, 2007 (12); Prospective Cohort Study; Germany; N: 4753	1-4, 5-6, 7-12mo	Atopic dermatitis (doctor-diagnosed and symptomatic) at 4y: No significant associations
Forsyth, 1993 (13); Prospective Cohort Study; Scotland; N: 392	<8, 8-12, >12wk	Atopic dermatitis between 53-104wk: 5.4% vs. 17% vs. 18%; $\chi 2 = 7.5$, P<0.05 Atopic dermatitis between 0-13, 14-26, 27-39, 40-52wk: No significant associations
Hesselmar, 2010 (1); Prospective Cohort Study; Sweden; N: 184	Age in months, continuous	Atopic dermatitis at 18mo: No significant associations
Illi, 2004 (14); Prospective Cohort Study; Germany; N: 858	Quartiles (not described)	Atopic dermatitis at 2y: No significant associations
Joseph, 2011 (15); Prospective Cohort Study; United States; N: 594	<4, >4mo	Atopic dermatitis at 2-3y: No significant associations
Kajosaari, 1983 (2); Prospective Cohort Study; Finland; N: 135	~3, 6mo	Atopic dermatitis at 1y: 35% vs.14%; P<0.001
Kajosaari, 1994 (3); Prospective Cohort Study; Finland; N: 135	~3, 6mo	Atopic dermatitis at 5y: No significant associations
Mihrshahi, 2007 (16); Prospective Cohort Study; Australia; N: 516	<3, >3mo	Atopic dermatitis at 5y: No significant associations

Reference[1]; Study design; Country; Sample size	Age of CFB introduction	Results
O'Donovan, 2016 (17); Prospective Cohort Study; United Kingdom; N: 709	<17, >26wk	Atopic dermatitis at 12mo: No significant associations
Poysa, 1989 (18); Prospective Cohort Study; Finland; N: 70	<3, 3-6, >6mo	Atopic dermatitis at 5y: No significant associations
Sandini, 2011 (6); Prospective Cohort Study; Finland; N: 925 at 2y, 891 at 5y	Categories not defined	Atopic dermatitis at 2y and 5y: No significant associations
Schoetzau, 2002 (19); Prospective Cohort Study; Germany; N: 1121	1-16, 17-24, >24wk	Atopic dermatitis at 1y: No significant associations
Snijders, 2008 (20); Prospective Cohort Study; The Netherlands; N: 2558	<3, 4-6, >7mo	Atopic dermatitis at 2y: 3 vs 4-6mo: OR=1.28, 95% CI: 0.91, 1.81); 3 vs >7mo: OR=2.1, 95% CI: 1.17, 3.76; P=0.02 Atopic dermatitis at 2y: 3 vs 4-6mo: OR=2.67, 95% CI: 0.80, 8.97; 3 vs > 7mo: OR=9.46, 95% CI: 2.05, 43.61; P=0.00
Taylor-Robinson, 2016 (21); Prospective Cohort Study; United Kingdom; N: 11537	<4, >4mo	Atopic dermatitis at 5y: OR=1.13, 95% CI: 1.04, 1.23
Van Asperen, 1984 (22); Prospective Cohort Study; Australia; N: 79	<4, >4mo	Atopic dermatitis at 20mo: No significant associations
Zutavern, 2006 (23); Prospective Cohort Study; Germany; N: 2612	0-4, 5-6, >6mo	Atopic dermatitis at 2y: No significant associations
Zutavern, 2008 (24); Prospective Cohort Study; Germany; N: 2073	<4, 4-6, >6mo	Atopic dermatitis at 6y: No significant associations
ASTHMA		
Fergusson, 1983 (26); Prospective Cohort Study; New Zealand; N: 1110	<4, >4mo	Asthma at 4y: No significant associations
Hetzner, 2009 (27); Prospective Cohort Study; United States; N: 7900	<6, >6mo	Asthma at 2y: No significant associations
Kajosaari, 1994 (3); Prospective Cohort Study; Finland; N: 135	~3, 6mo	Asthma at 5y: No significant associations
Mihrshahi, 2007 (16); Prospective Cohort Study; Australia; N: 516	<3, >3mo	Asthma at 5y: No significant associations

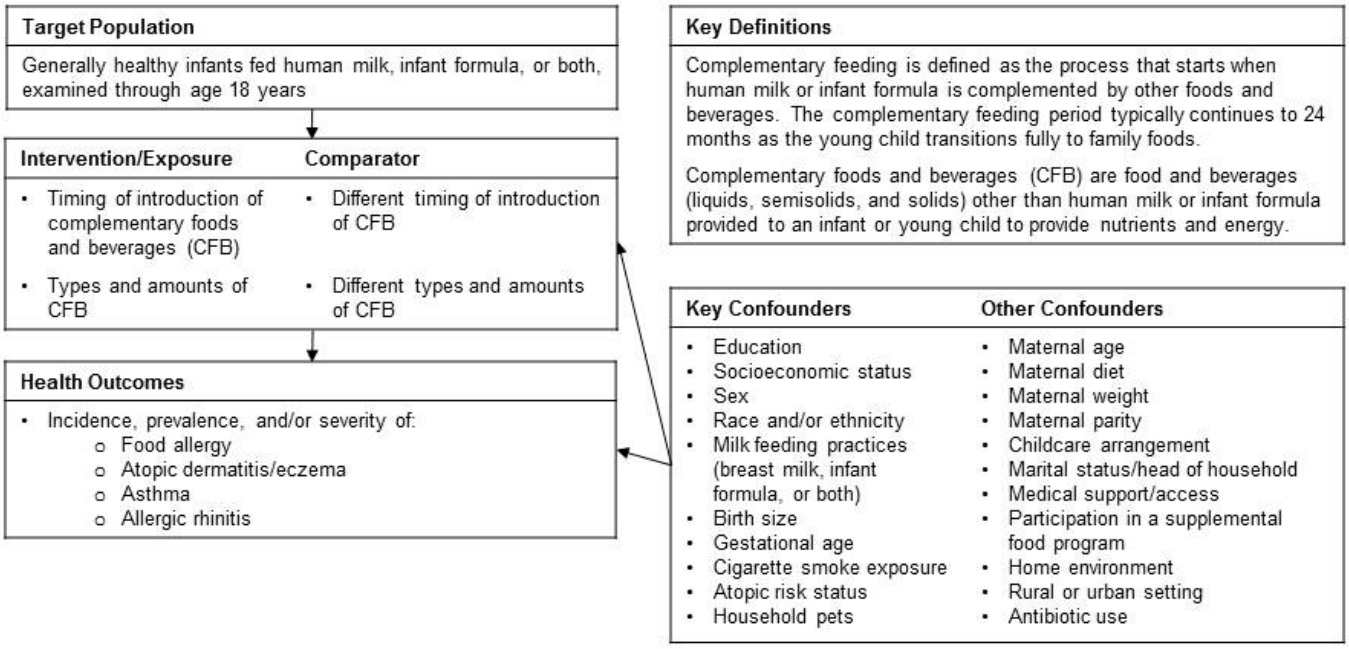
Reference[1]; Study design; Country; Sample size	Age of CFB introduction	Results
Nathan, 2012 (28); Case-Control Study; Malaysia; Asthma Cases: 78, Controls: 78	<6, >6mo	Asthma cases vs.controls: 65% vs. 33%; P<0.001
Sandini, 2011 (6); Prospective Cohort Study; Finland; N: 925 at 2y, 891 at 5y	Categories not defined	Asthma at 2y and 5y: No significant associations
Wilson, 1998 (29); Prospective Cohort Study; Australia; N: 545	: <15, >15wk	Asthma at ~7y: No significant associations
Zutavern, 2008 (24); Prospective Cohort Study; Germany; N: 2073	<4, 4-6, >6mo	Asthma at 6y: No significant associations
ALLERGIC RHINITIS		
Kajosaari, 1994 (3); Prospective Cohort Study; Finland; N: 135	~3, 6mo	Allergic rhinitis at 5y: 37% vs. 20%; P=0.04
Sandini, 2011 (6); Prospective Cohort Study; Finland; N: 925 at 2y, 891 at 5y	Categories not defined	Allergic rhinitis at 2y and 5y: No significant associations
Van Asperen, 1984 (22); Prospective Cohort Study; Australia; N: 79	<4, >4mo	Allergic rhinitis at 20mo: No significant associations
Zutavern, 2008 (24); Prospective Cohort Study; Germany; N: 2073	<4, 4-6, >6mo	Allergic rhinitis at 6y: No significant associations
ATOPIC DISEASE		
Kajosaari, 1994 (3); Prospective Cohort Study; Finland; N: 135	~3, 6mo	Atopic disease at 5y: No significant associations
Poysa, 1991 (30); Prospective Cohort Study; Finland; N: 68	<3, 3-6, >6mo	Atopic disease at 9y: No significant associations
Yung, 2015 (31); Case-Control Study; China (Hong Kong); Atopic Cases: 71, Controls: 135	Categories not defined	Atopic disease, cases vs. controls: No significant associations

[1]References may be repeated if reporting multiple different outcomes in relation to the age when complementary feeding began

ANALYTIC FRAMEWORK

The analytic framework (Figure 1) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The analytic framework in Figure 1 is for systematic reviews conducted to examine the relationship between complementary feeding and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis

Figure 1: Analytic framework



SEARCH PLAN AND RESULTS

Inclusion and exclusion criteria

The inclusion and exclusion criteria are a set of characteristics to determine which studies will be included or excluded in the systematic review. This table provides the inclusion and exclusion criteria for the systematic review question(s): What is the relationship between timing of introduction of complementary foods/beverages or types and amounts of complementary foods/beverages and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis?

Table 3. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
Study design	Randomized controlled trials	Cross-sectional studies

Category	Inclusion Criteria	Exclusion Criteria
	Non-randomized controlled trials	Uncontrolled studies
	Prospective cohort studies	Pre/post studies without a control
	Retrospective cohort studies	Narrative reviews
	Case-control studies	Systematic reviews
	Pre/post studies with a control	Meta-analyses
Independent variable (intervention or exposure)	Timing of introduction to complementary foods and beverages (CFB) (i.e., foods and beverages (liquids, semisolids, and solids) other than human milk or infant formula provided to an infant or young child to provide nutrients and energy)	Consumption of fluid cow's milk before 12 months of age
	Types or amounts of CFB	
Comparator	Different timing of introduction of CFB	
	Different types and amounts of CFB	
Dependent variables (outcomes)	Incidence, prevalence, and/or severity of: food allergy, atopic dermatitis/eczema, asthma, and/or allergic rhinitis	Food allergy when diagnosis was based solely on food allergen sensitization (i.e., skin prick test, or serum IgE measure)
		Asthma when diagnosis was based solely on report of wheeze
Date range	January 1980 – February 2017	
Language	Studies published in English	Studies published in languages other than English
Publication status	Studies published in peer-reviewed journals	Grey literature, including unpublished data, manuscripts, reports, abstracts, conference proceedings
Country[1, 2, 3]	Studies conducted in Very High or High Human Development Countries	Studies conducted in Medium or Low Human Development Countries
Study participants	Human subjects	Hospitalized patients, not including birth and immediate post-partum hospitalization of healthy babies
	Males	
	Females	
Age of study participants	Age at intervention or exposure: Infants (0-12mo); Toddlers (12-24mo)	Age at intervention or exposure: Child (2-5 years (y)); Child (6-12y); Adolescents (13-18y); Adults (19y and older); Older adults (65 to 79y); Older adults (80+y)
	Age at outcome: Infants (0-12mo; food allergy, atopic dermatitis, allergic rhinitis); Toddlers (12-24mo; food allergy, atopic dermatitis, allergic rhinitis); Child (2-5 years (y)); Child (6-12y); Adolescents (13-18y)	Age at outcome: Infants (0-12 months) (asthma); Toddlers (12-24 months) (asthma); Adults (19y and older); Older adults (65 to 79y); Older adults (80+y)
Health status of study participants	Studies done in generally healthy populations	Studies that exclusively enroll subjects with a disease or with the health outcome of interest

Category	Inclusion Criteria	Exclusion Criteria
	Studies done in populations where infants were full term (≥37wk gestational age)	Studies done in hospitalized or malnourished subjects
	Studies done in populations with elevated chronic disease risk, or that enroll some participants with a disease or with the health outcome of interest	Studies of exclusively pre-term babies (gestational age <37wk) or babies that are small for gestational age (<2500g)
		Studies of subjects with infectious diseases (e.g. HIV/AIDS) (or with mothers diagnosed with an infectious disease)

[1] United Nations Development Programme. Human Development Report 2014: Reducing Vulnerabilities and Building Resilience. Available from: http://hdr.undp.org/en/content/human-development-report-2014. (32)

[2] Medium Development Countries were originally included, but due to concerns about generalizability to the U.S. of study participants (i.e., baseline health status) and CFB typically consumed, a decision was made to exclude "Medium" countries in October 2017.

[3] When a country was not included in the Human Development Report 2014, country classification from the World Bank was used instead. (33)

Search terms and electronic databases used

PubMed, US National Library of Medicine (1966 to 8 February 2017):
Date(s) Searched: 2/8/2017
Search Terms:
Date range searched: 1980-2/8/17

(Complementary OR supplementary OR wean* OR transition* OR introduc* OR "Infant Nutritional Physiological Phenomena"[Mesh:noexp] OR weaning[mesh] OR bottle*)

AND (feeding* OR food* OR beverage*[tiab] OR beverages[mh] OR eating OR diet[tiab] OR diet[mh] OR meal*[tiab] OR meals[mh] OR "Food and Beverages"[Mesh] OR diets[tiab] OR cereal*[tiab] OR "Edible Grain"[Mesh] OR bread*[tiab] OR whole grain* OR juice*[tiab] OR milk[tiab] OR "Milk"[Mesh] OR dairy[tiab] OR "Dairy Products"[Mesh] OR meat[tiab] OR cheese[tiab] OR yogurt[tiab] OR yoghurt*[tiab] OR fruit*[tiab] OR "Fruit"[Mesh] OR vegetable*[tiab] OR "Vegetables"[Mesh] OR egg*[tiab] OR "Eggs"[Mesh] OR nut[tiab] OR nuts[tiab] OR peas[tiab] OR beans[tiab] OR legume*[tiab] OR snack*[tiab] OR bread[mh] OR honey[mh] OR vegetable*[tiab] OR "Vegetables"[Mesh] OR egg*[tiab] OR "Eggs"[Mesh:noexp] OR "egg white"[mh] OR "egg yolk"[mh] OR snack*[tiab] OR candy[mh] OR "Fast Foods"[Mesh] OR meat[mh] OR molasses[mh] OR nuts[mh] OR "Raw Foods"[Mesh] OR seeds[mh])

OR
"infant food"[mesh] OR infant feed* OR Bottle feeding[mh] OR bottle feeding*[tiab] OR bottle feeding OR bottle-feeding*[tiab] OR bottle-feedings OR bottle-fed[tiab] OR "bottle fed"[tiab] OR solid food*

AND

NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic[sb])

("Study Characteristics" [Publication Type] OR “clinical trial”[ptyp] OR "Epidemiologic Studies"[Mesh] OR "Support of Research"[ptyp] OR cohort[tiab] OR observational[tiab] OR retrospective[tiab] OR longitudinal[tiab] OR trial[tiab] OR trials[tiab] OR case control*[tiab] OR case-control*[tiab] OR before-after stud*[tiab] OR before after stud*[tiab]

(includes age filter: Filters: Infant: birth-23 months and preschool child 2-5 yrs)

OR ((Solid food*) OR solids))

AND

(("Allergy and Immunology"[Mesh:NoExp] OR allergy[tiab] OR allergies[tiab] OR allergic[tiab] OR Hypersensitivit*[tiab]) AND (food OR peanut* OR nut OR nuts OR egg OR eggs OR milk OR shellfish OR wheat)) OR "Food Hypersensitivity"[Mesh] OR asthma OR "Rhinitis, Allergic"[Mesh] OR (allergic[tiab] AND Rhiniti*[tiab]) OR "Dermatitis, Atopic"[Mesh] OR ((Dermatiti*[tiab] OR eczema[tiab]) AND Atopic[tiab]) OR (Infant* AND Eczema) OR "Immunoglobulin E"[Mesh] OR "Immunoglobulin E"[tiab] OR IgE[tiab]

for nonmedline[sb]: NOT animals by: NOT (sheep[ti] OR lamb[ti] OR lambs[ti] OR calving[ti] OR calves[ti] OR mice[ti] OR mouse[ti] OR pigs[ti] OR cows[ti] OR piglets[ti] OR cow[ti] OR piglet[ti] OR monkey[ti] OR rats[ti] OR rat[ti] OR animal*[ti])

infant* OR baby OR babies OR toddler* OR newborn*[tiab] OR "Child, Preschool"[Mesh] OR preschool*[tiab] OR pre-school*[tiab] OR “early childhood”[tiab] OR early year*[tiab] OR pre-k[tiab] OR pre-primary[tiab] OR under five*[ti] OR young child*[ti] OR prekindergarten[tiab] OR pre-kindergarten[tiab] OR weanling* OR “first two years” OR “first 2 years”

Embase, Elsevier (1947 to February 2017):

Date(s) Searched: 2/2017
Search Terms:

'complementary feeding'/exp OR

(Complementary OR supplementa* OR wean* OR transition* OR introduc* OR family) NEAR/3 (feed* OR food* OR beverage* OR eating OR diet)

OR
(Complementary OR transition* OR introduct* OR wean*) AND (food/exp OR 'baby food'/exp OR 'cereal'/exp OR 'dairy product'/exp OR 'egg'/exp OR 'fruit'/exp OR

'meat'/exp OR 'sea food'/exp OR 'milk'/exp OR fish/exp OR 'poultry'/exp OR 'beverage'/exp OR 'vegetable'/exp OR nut/exp OR pea/exp OR meal/exp OR 'infant feeding'/exp)

OR
(Complementary OR supplementa* OR wean* OR transition* OR introduc*) NEAR/5 ('whole grain' OR 'whole grains' OR dairy OR egg OR eggs OR meat OR poultry OR seafood OR fruit* OR milk OR fish* OR poultry OR beverage* OR vegetables* OR pea OR peas OR nut OR nuts OR cereal OR bread* OR yog*urt* OR cheese* OR juice* OR rice OR soup OR legume* OR snack* OR meal*)

OR 'baby food'/de OR (solid NEAR/2 food*):ab,ti

AND
(infant*:ti,ab OR infant/exp) OR (baby OR babies OR toddler* OR newborn* OR nurser*):ti,ab OR 'newborn'/exp OR 'newborn care'/exp OR preschool*:ti,ab OR pre-school:ti,ab OR 'preschool child'/exp OR 'infancy'/exp OR "early childhood":ti,ab OR "early years" OR pre-k:ti,ab OR 'nursery'/exp OR 'nursery school'/exp OR prekindergarten:ti,ab OR pre-kindergarten:ti,ab OR weanling* (includes limits below) OR ([newborn]/lim OR [infant]/lim OR [child]/lim OR [preschool]/lim)

AND ([in process]/lim OR [article]/lim OR [article in press]/lim) AND ([embase]/lim NOT [medline]/lim)

Limit to humans:

AND

'allergic asthma'/exp OR 'food allergy'/exp OR 'allergic rhinitis'/exp OR 'dermatitis'/exp OR 'eczema'/exp OR 'skin allergy'/exp OR ((allerg* OR hypersensitivity*) NEAR/3 (food OR peanut* OR nut OR nuts OR egg OR milk OR shellfish OR wheat)) OR 'immunoglobulin E'/exp OR 'immunoglobulin E':ti,ab OR 'atopy'/exp OR atopy:ti,ab OR atopic:ti,ab OR IgE:ti,ab

Cochrane Central Register of Controlled Trials, John Wiley & Sons in the Cochrane Library (searched 9 February 2017):
Date(s) Searched: 2/9/17
Search Terms:

(feed* OR food* OR beverage*OR diet* OR 'whole grain' OR 'whole grains' OR dairy OR egg OR meat OR poultry OR seafood OR fruit* OR milk OR fish* OR poultry OR vegetables* OR pea OR beans OR legume* OR nut OR cereal OR beverage* OR bread* OR seafood OR yog*urt* OR cheese OR juice OR snack OR yogurt OR yoghurt OR nut OR nuts OR honey OR meal OR meals) NEAR/3 (Complementary OR supplementa* OR wean* OR transition* OR introduct* OR family)

OR

[mh ^"Infant Nutritional Physiological Phenomena"] OR [mh weaning] OR ((bottle*) NOT (milk OR formula))
AND ([mh beverages] OR [mh eating] OR [mh diet] OR [mh meals] OR [mh "Food and Beverages"] OR [mh "Edible Grain"] OR [mh "Milk"] OR dairy:ti,ab OR [mh "Dairy Products"] OR [mh "Fruit"] OR [mh "Vegetables"] OR [mh "Eggs"] OR [mh bread] OR [mh honey] OR [mh "Vegetables"] OR [mh ^"Eggs"] OR [mh “egg white”] OR [mh “egg yolk”] OR [mh candy] OR [mh "Fast Foods"] OR [mh meat] OR [mh molasses] OR [mh nuts] OR [mh "Raw Foods"] OR [mh seeds])

OR
((Infant* OR baby* OR babies) NEAR/2 food*):ti,ab OR [mh "infant food"]

AND

[mh ^"Allergy and Immunology"] OR ((allerg*:ti,ab OR Hypersensitivit*:ti,ab) AND (food OR peanut OR nut OR nuts OR egg OR milk OR shellfish OR wheat)) OR [mh "Food Hypersensitivity"] OR asthma* OR [mh" Rhinitis, Allergic"] OR (allerg* NEAR/5 Rhiniti*) OR [mh "Dermatitis, Atopic"] OR ((Dermatiti* OR eczema) NEAR/5 Atopic) OR (Infant* NEAR/5 Eczema) OR [mh "Immunoglobulin E"] OR "Immunoglobulin E”:ti,ab OR IgE:ti,ab

CINAHL Plus with Full Text, EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1937 to 9 February 2017):
Date(s) Searched: 2/9/17
Search Terms:
209; selected 26 for downloading

(MH "Food Hypersensitivity+") OR (MH "Milk Hypersensitivity") OR (MH "Pollen-Food Allergy") OR (MH "Rhinitis, Atrophic") OR "Immunoglobulin e" OR (MH "Eczema") OR (MH "Dermatitis, Atopic")

AND

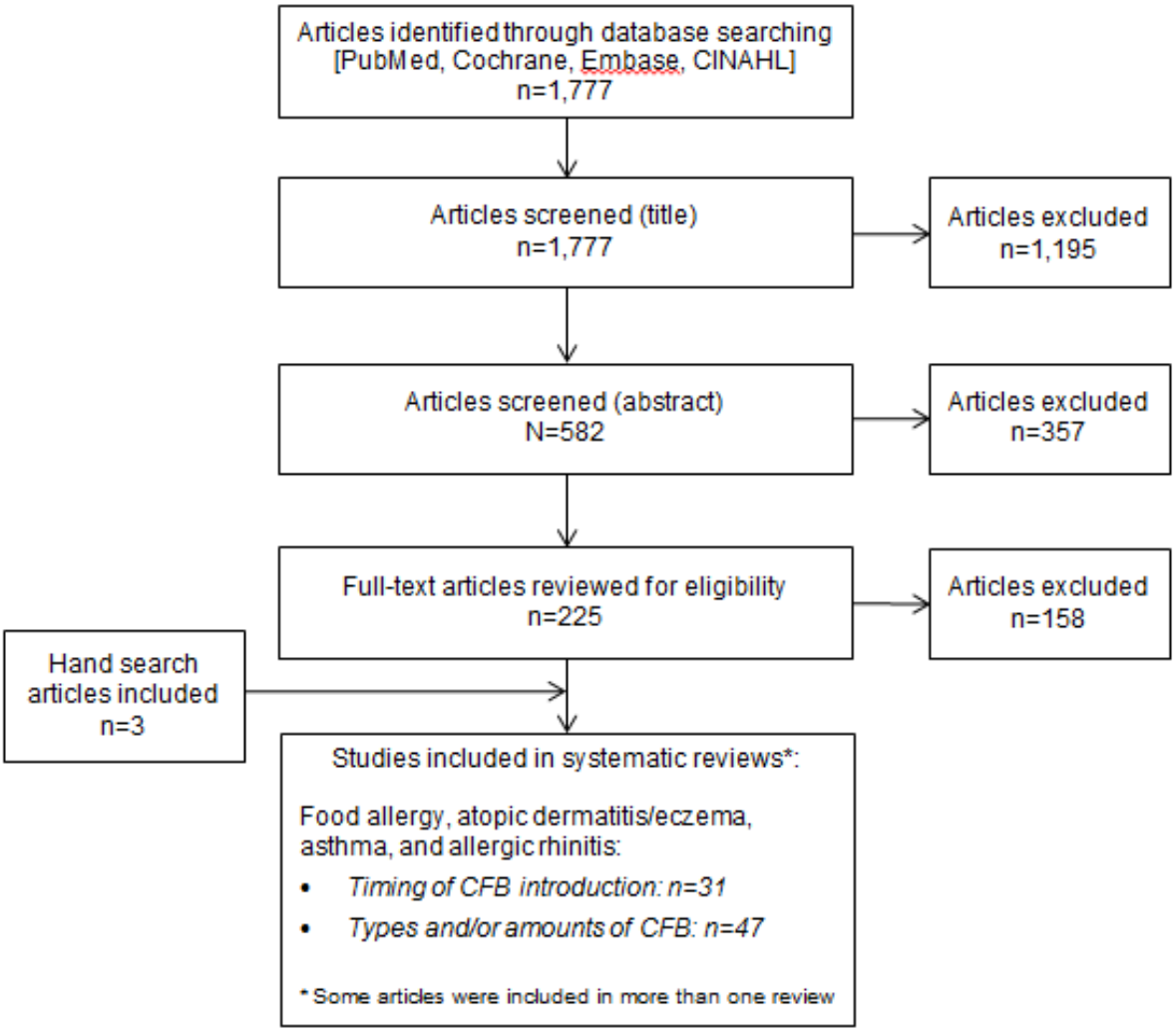
(MH "Food and Beverages+") OR (MH "Food") OR (MH "Diet") OR (MH "Eating") OR (MH "Eating Behavior") OR (MH "Taste") OR (MH "Taste Buds") OR (MH "Cereals") OR (MH "Dairy Products") OR (MH "Yogurt") OR (MH "Cheese") OR (MH "Milk") OR (MH "Eggs") OR (MH "Fruit") OR (MH "Fruit Juices") OR (MH "Meat") OR (MH "Seafood") OR (MH "Fish") OR (MH "Poultry") OR (MH "Vegetables") OR (MH "Nuts") OR (MH "Legumes") OR (MH "Bread") AND (Complementary OR supplementa* OR wean* OR transition* OR introduc*)

OR
(‘whole grain’ OR ‘whole grains’ OR dairy OR egg OR eggs OR meat OR poultry OR seafood OR fruit* OR milk OR fish* OR poultry OR vegetables* OR pea OR peas OR nut OR nuts OR cereal OR beverage* OR bread* OR seafood OR yog*urt* OR cheese* OR juice*) N5 (Complementary OR supplementa* OR wean* OR transition*

OR introduc* OR family)

OR (Infant* OR baby OR babies) N3 food*

Figure 2: Flow chart of literature search and screening results



This flow chart illustrates the literature search and screening results for articles examining the relationship between complementary feeding and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis. The results of the electronic database searches were screened independently by two NESR analysts in a step-wise manner by reviewing titles, abstracts, and full text articles to determine which articles met the criteria for inclusion. A manual search was done to ascertain articles not identified through the electronic database search. The systematic review on timing of CFB introduction included 31 articles, and the systematic review on on types and amounts of CFB consumed included 47 articles.

Excluded articles

The table below lists the excluded articles with at least one reason for exclusion, and may not reflect all possible reasons.

Table 4. Excluded articles

	Citation	Reasons for Exclusion
1	Children's peanut allergies arising at younger ages. AORN Journal. 2008;87:624-624.	Study design
2	Infants with food protein allergy tolerate soy milk earlier than cow's. Community Practitioner. 2009;82:41-41.	Study design
3	Significance of food hypersensitivity in children with atopic dermatitis. Pediatr Dermatol. 1986;3:161-74.	Study design
4	Aberg, N.,Engstrom, I.,Lindberg, U.. Allergic diseases in Swedish school children. Acta Paediatr Scand. 1989;78:246-52.	Study design
5	Abrams, E. M.,Becker, A. B.. Introducing solid food: age of introduction and its effect on risk of food allergy and other atopic diseases. Can Fam Physician. 2013;59:721-2.	Study design
6	Alper, Z.,Sapan, N.,Ercan, I.,Canitez, Y.,Bilgel, N.. Risk factors for wheezing in primary school children in Bursa, Turkey. Am J Rhinol. 2006;20:53-63.	Study design
7	Armentia, A.,Rodriguez, R.,Callejo, A.,Martin-Esteban, M.,Martin-Santos, J. M.,Salcedo, G.,Pascual, C.,Sanchez-Monge, R.,Pardo, M.. Allergy after ingestion or inhalation of cereals involves similar allergens in different ages. Clin Exp Allergy. 2002;32:1216-22.	Health Status, Independent Variable
8	Arshad, S. H.,Matthews, S.,Gant, C.,Hide, D. W.. Effect of allergen avoidance on development of allergic disorders in infancy. Lancet. 1992;339:1493-7.	Independent Variable
9	Bardara, M.,Varin, E.,Zani, G.. Response to diet in 130 children affected with atopic dermatitis. Allergy. 1989:147-50.	Study design
10	Bardare, M.,Vaccari, A.,Allievi, E.,Brunelli, L.,Coco, F.,de Gaspari, G. C.,Flauto, U.. Influence of dietary manipulation on incidence of atopic disease in infants at risk. Ann Allergy. 1993;71:366-71.	Independent Variable
11	Becker, A.,Watson, W.,Ferguson, A.,Dimich-Ward, H.,Chan-Yeung, M.. The Canadian asthma primary prevention study: outcomes at 2 years of age. J Allergy Clin Immunol. 2004;113:650-6.	Study design, Independent Variable
12	Benn, C. S.,Wohlfahrt, J.,Aaby, P.,Westergaard, T.,Benfeldt, E.,Michaelsen, K. F.,Bjorksten, B.,Melbye, M.. Breastfeeding and risk of atopic dermatitis, by parental history of allergy, during the first 18 months of life. Am J Epidemiol. 2004;160:217-23.	Independent Variable
13	Berg, Av,Kramer, U.,Link, E.,Bollrath, C.,Heinrich, J.,Brockow, I.,Koletzko, S.,Grubl, A.,Filipiak-Pittroff, B.,Wichmann, H. E.,Bauer, C. P.,Reinhardt, D.,Berdel, D.. Impact of early feeding on childhood eczema:	Independent Variable

	Citation	Reasons for Exclusion
	development after nutritional intervention compared with the natural course - the GINIplus study up to the age of 6 years. Clin Exp Allergy. 2010;40:627-36.	
14	Bergmann, R. L.,Bergmann, K. E.,Lau-Schadensdorf, S.,Luck, W.,Dannemann, A.,Bauer, C. P.,Dorsch, W.,Forster, J.,Schmidt, E.,Schulz, J.,et, al. Atopic diseases in infancy. The German multicenter atopy study (MAS-90). Pediatr Allergy Immunol. 1994;5:19-25.	Independent Variable
15	Bilenko, N.,Ghosh, R.,Levy, A.,Deckelbaum, R. J.,Fraser, D.. Partial breastfeeding protects Bedouin infants from infection and morbidity: prospective cohort study. Asia Pac J Clin Nutr. 2008;17:243-9.	Independent Variable
16	Bion, V.,Lockett, G. A.,Soto-Ramírez, N.,Zhang, H.,Venter, C.,Karmaus, W.,Holloway, J. W.,Arshad, S. H.. Evaluating the efficacy of breastfeeding guidelines on long-term outcomes for allergic disease. Allergy: European Journal of Allergy and Clinical Immunology. 2016;71:661-670.	Independent Variable
17	Birkbeck, J. A.. Goat milk in infant nutrition. N Z Med J. 1984;97:413-4.	Study design
18	Blumberg, S.. Infant feeding: can we spice it up a bit?. J Am Diet Assoc. 2006;106:504-5.	Study design
19	Bruno, G.,Milita, O.,Ferrara, M.,Nisini, R.,Cantani, A.,Businco, L.. Prevention of atopic diseases in high risk babies (long-term follow-up). Allergy Proc. 1993;14.	Independent Variable
20	Burks, K.,Jones, S.. The Canadian asthma primary prevention study: Outcomes at 2 years of age. Pediatrics. 2005;116:537-4005.	Study design
21	Burr, M. L.,Limb, E. S.,Maguire, M. J.,Amarah, L.,Eldridge, B. A.,Layzell, J. C.,Merrett, T. G.. Infant feeding, wheezing, and allergy: a prospective study. Arch Dis Child. 1993;68:724-8.	Independent Variable
22	Burr, M. L.,Merrett, T. G.,Dunstan, F. D.,Maguire, M. J.. The development of allergy in high-risk children. Clin Exp Allergy. 1997;27:1247-53.	Independent Variable
23	Calamaro, C. J.. Infant nutrition in the first year of life: tradition or science?. Pediatr Nurs. 2000;26:211-5.	Study design
24	Cant, A. J.,Bailes, J. A.. How should we feed the potentially allergic infant?. Hum Nutr Appl Nutr. 1984;38:474-6.	Study design
25	Challacombe, D. N.. Allergies and infant feeding. Midwife Health Visit Community Nurse. 1986;22:164-6.	Study design
26	Chandra, R. K.. Role of maternal diet and mode of infant feeding in prevention of atopic dermatitis in high risk infants. Allergy. 1989:135-9.	Study design
27	Chiu, C. Y.,Liao, S. L.,Su, K. W.,Tsai, M. H.,Hua, M. C.,Lai, S. H.,Chen, L. C.,Yao, T. C.,Yeh, K. W.,Huang, J. L.. Exclusive or Partial Breastfeeding for 6 Months Is Associated with Reduced Milk Sensitization and Risk of Eczema in Early Childhood. Medicine (United States). 2016;95.	Independent Variable
28	Cho, H. N.,Hong, S.,Lee, S. H.,Yum, H. Y.. Nutritional status according to sensitized food allergens in children with atopic dermatitis. Allergy Asthma Immunol Res. 2011;3:53-7.	Study design

	Citation	Reasons for Exclusion
29	Cudowska, B.,Marcinkiewicz, S.,Kaczmarski, M.. Sensitization to cereal allergens in children with atopic dermatitis. Postepy Dermatologii i Alergologii. 2011;28:181-186.	Study design, Health Status
30	de Looy, A. E.. Infant nutrition. Nursing (Lond). 1986;3:446-9.	Study design
31	del-Rio Camacho, G.,Martinez Jimenez, V.,Fernandez-Cantalejo Padial, J.. Absence of clinical symptoms upon introduction of egg into the diet of milk-allergic infants not previously sensitised to egg. Allergol Immunopathol (Madr). 2012;40:374-8.	Health Status, Independent Variable
32	Dieguez, M. C.,Cerecedo, I.,Muriel, A.,Zamora, J.,Sanchez-Cano, M.,De la Hoz, B.. Skin prick test predictive value on the outcome of a first known egg exposure in milk-allergic children. Pediatr Allergy Immunol. 2008;19:319-24.	Health Status, Independent Variable
33	Du Toit, G.,Katz, Y.,Sasieni, P.,Mesher, D.,Maleki, S. J.,Fisher, H. R.,Fox, A. T.,Turcanu, V.,Amir, T.,Zadik-Mnuhin, G.,Cohen, A.,Livne, I.,Lack, G.. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. J Allergy Clin Immunol. 2008;122:984-91.	Study design, Dependent Variable
34	Dubakiene, R.,Rudzeviciene, O.,Butiene, I.,Sezaite, I.,Petronyte, M.,Vaicekauskaite, D.,Zvirbliene, A.. Studies on early allergic sensitization in the Lithuanian birth cohort. ScientificWorldJournal. 2012;2012:909524.	Independent Variable
35	Duczmal, E.,Breborowicz, A.,Duczmal, T.. The influence of specific factors on the prevalence of allergic diseases in a birth cohort study [polish]. Alergia Astma Immunologia. 2011;16:96-104.	Language
36	Dunlop, A. L.,Reichrtova, E.,Palcovicova, L.,Ciznar, P.,Adamcakova-Dodd, A.,Smith, S. J.,McNabb, S. J.. Environmental and dietary risk factors for infantile atopic eczema among a Slovak birth cohort. Pediatr Allergy Immunol. 2006;17:103-11.	Study design
37	Early peanut consumption may prevent allergy. Nurse Prescribing. 2008;6:509-509.	Study design
38	Exl, B. M.,Deland, U.,Secretin, M. C.,Preysch, U.,Wall, M.,Shmerling, D. H.. Improved general health status in an unselected infant population following an allergen-reduced dietary intervention programme: the ZUFF-STUDY-PROGRAMME. Part II: infant growth and health status to age 6 months. ZUg-FrauenFeld. Eur J Nutr. 2000;39:145-56.	Independent Variable
39	Fadeeva, T.,Asin, J. L.,Horrillo, M. L.,Baraut, T. G.,Vela, R. F.,Conde, S. L.,Hontoria, O. E.,Valero, C. B.,Molina, A. M.. Results of the oral egg-challenge test performed on two different groups of children. One group with a history, suggestive of allergic reaction with egg intake and the other group sensitised to hen's egg without previous egg intake. Allergol Immunopathol (Madr). 2010;38:233-40.	Independent Variable
40	Filipiak, B.,Zutavern, A.,Koletzko, S.,Von Berg, A.,Brockow, I.,Grübl, A.,Berdel, D.,Reinhardt, D.,Bauer, C. P.,Wichmann, H. E.,Heinrich, J.. Early solid food introduction and development of eczema in the first 4 years. Results from the GINI birth cohort. Allergo Journal. 2008;17:82-83.	Language
41	Fiocchi, A.,Verga, M. C.. Early allergenic-food introduction does not reduce subsequent food allergy development. J Pediatr. 2016;178:305-306.	Study design

	Citation	Reasons for Exclusion
42	Flohr, C.,Nagel, G.,Weinmayr, G.,Kleiner, A.,Strachan, D. P.,Williams, H. C.. Lack of evidence for a protective effect of prolonged breastfeeding on childhood eczema: lessons from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. Br J Dermatol. 2011;165:1280-9.	Study design
43	Frank, L.,Marian, A.,Visser, M.,Weinberg, E.,Potter, P. C.. Exposure to peanuts in utero and in infancy and the development of sensitization to peanut allergens in young children. Pediatr Allergy Immunol. 1999;10:27-32.	Country
44	Gabet, S.,Just, J.,Couderc, R.,Seta, N.,Momas, I.. Allergic sensitisation in early childhood: Patterns and related factors in PARIS birth cohort. Int J Hyg Environ Health. 2016;219:792-800.	Dependent Variable
45	Geller-Bernstein, G.,Kenett, R.,Weisglass, L.,Tsur, S.,Lahav, M.,Levin, S.. Atopic babies with wheezy bronchitis. Follow-up study relating prognosis to sequential IgE values, type of early infant feeding, exposure to parental smoking and incidence of lower respiratory tract infections. Allergy. 1987;42:85-91.	Health Status, Independent Variable
46	Ghaderi, R.,Makhmalbaf, Z.. Effect of breast-feeding on the development of atopic dermatitis. Iranian Journal of Allergy, Asthma and Immunology. 2005;4:129-132.	Independent Variable
47	Ghadi, A.,Dutau, G.,Rancé, F.. A sensitization study of atopic children in Marrakech. A prospective study of 160 children between 2002 and 2005 [french]. Revue Francaise d'Allergologie et d'Immunologie Clinique. 2007;47:409-415.	Language
48	Gray, C. L.,Levin, M. E.,du Toit, G.. Patterns of introduction of solids in South African children with atopic dermatitis: Do they affect allergy rates?. Current Allergy and Clinical Immunology. 2014;27:334-336.	Study design, Health Status
49	Greenhawt, M.,Venter, C.. Having your cake and EATing it too: early timing of multiple allergen introduction does not increase the risk of developing food allergy in standard risk, breastfed infants. Evid Based Med. 2017.	Study design
50	Greenhawt, M.. Early Allergen Introduction for Preventing Development of Food Allergy [editorial]. Jama. 2016;316:1157-1159.	Study design
51	Greenhawt, M.. Early Allergen Introduction for Preventing Development of Food Allergy. Jama. 2016;316:1157-1159.	Study design
52	Guilbert, T. W.,Stern, D. A.,Morgan, W. J.,Martinez, F. D.,Wright, A. L.. Effect of breastfeeding on lung function in childhood and modulation by maternal asthma and atopy. Am J Respir Crit Care Med. 2007;176:843-8.	Independent Variable
53	Gupta, R. S.,Walkner, M. M.,Greenhawt, M.,Lau, C. H.,Caruso, D.,Wang, X.,Pongracic, J. A.,Smith, B.. Food Allergy Sensitization and Presentation in Siblings of Food Allergic Children. Journal of Allergy and Clinical Immunology: In Practice. 2016;4:956-962.	Health Status, Independent Variable
54	Halken, S.,Host, A.,Hansen, L. G.,Osterballe, O.. Effect of an allergy prevention programme on incidence of atopic symptoms in infancy. A prospective study of 159 "high-risk" infants. Allergy. 1992;47:545-53.	Independent Variable
55	Halken, S.. What causes allergy and asthma? The role of dietary factors. Pediatr Pulmonol Suppl. 2004;26:223-4.	Study design

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56	Hartman, H.,Dodd, C.,Rao, M.,DeBlasio, D.,Labowsky, C.,D'Souza, S.,Lenkauskas, S.,Roeser, E.,Heffernan, A.,Assa'ad, A.. Parental timing of allergenic food introduction in urban and suburban populations. Ann Allergy Asthma Immunol. 2016;117.	Dependent Variable
57	Hill, D. J.,Hosking, C. S.. Preventing childhood allergy. Med J Aust. 1993;158:367-9.	Study design
58	Holmes, S.. Planning for the best start in life. A guide to infant feeding. Prof Nurse. 1991;6:200-5.	Study design
59	Hon, K. L. E.,Tsang, Y. C.,Poon, T. C. W.,Pong, N. H. H.,Luk, N. M.,Leung, T. N. H.,Chow, C. M.,Leung, T. F.. Dairy and nondairy beverage consumption for childhood atopic eczema: What health advice to give?. Clinical and Experimental Dermatology. 2016;41:129-137.	Study design, Age
60	Horwitz, A. A.,Hossain, J.,Yousef, E.. Correlates of outcome for atopic dermatitis. Ann Allergy Asthma Immunol. 2009;103:146-51.	Study design, Health Status
61	Howie, P. W.,Forsyth, J. S.,Ogston, S. A.,Clark, A.,Florey, C. D.. Protective effect of breast feeding against infection. Bmj. 1990;300:11-6.	Independent Variable
62	Hua, M. C.,Chen, C. C.,Liao, S. L.,Yao, T. C.,Tsai, M. H.,Lai, S. H.,Chiu, C. Y.,Yeh, K. W.,Huang, J. L.. Faecal eosinophil cationic protein and serum immunoglobulin E in relation to infant feeding practices. Ann Clin Biochem. 2016.	Dependent Variable
63	Ito, J.,Fujiwara, T.. Breastfeeding and risk of atopic dermatitis up to the age 42 months: a birth cohort study in Japan. Ann Epidemiol. 2014;24:267-72.	Independent Variable
64	Juto, P.,Bjorksten, B.. Serum IgE in infants and influence of type of feeding. Clin Allergy. 1980;10:593-600.	Independent Variable
65	Juto, P.,Moller, C.,Engberg, S.,Bjorksten, B.. Influence of type of feeding on lymphocyte function and development of infantile allergy. Clin Allergy. 1982;12:409-16.	Independent Variable
66	Kajosaari, M.. Atopy prophylaxis in high-risk infants. Prospective 5-year follow-up study of children with six months exclusive breastfeeding and solid food elimination (not peer review). Adv Exp Med Biol. 1991;310:453-8.	Study design
67	Kaufman, H. S.,Frick, O. L.. Prevention of asthma. Clin Allergy. 1981;11:549-53.	Independent Variable
68	Khoo, P.,Boyce, S.. Does early introduction of allergenic foods decrease the risk of food allergies?. J Paediatr Child Health. 2016;52:850.	Study design
69	Kiefte-de Jong, J. C.,de Vries, J. H.,Franco, O. H.,Jaddoe, V. W.,Hofman, A.,Raat, H.,de Jongste, J. C.,Moll, H. A.. Fish consumption in infancy and asthma-like symptoms at preschool age. Pediatrics. 2012;130:1060-8.	Dependent Variable
70	Kiefte-de Jong, J. C.,Escher, J. C.,Arends, L. R.,Jaddoe, V. W.,Hofman, A.,Raat, H.,Moll, H. A.. Infant nutritional factors and functional constipation in childhood: the Generation R study. Am J Gastroenterol. 2010;105:940-5.	Dependent Variable

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71	Kim, J.,Chung, Y.,Han, Y.,Ahn, K.,Lee, S. I.. The natural history and prognostic factors of egg allergy in Korean infants with atopic dermatitis. Asian Pac J Allergy Immunol. 2009;27:107-14.	Health Status
72	Kmietowicz, Zosia. Risk of peanut allergy can be reduced by 80% by including peanuts in infant diets. BMJ: British Medical Journal. 2015;350.	Study design
73	Koletzko, B.. Complementary foods and the development of food allergy. Pediatrics. 2000;106:1285.	Study design
74	Koletzko, S.. 2.5 Allergy Prevention through Early Nutrition. World Rev Nutr Diet. 2015;113:113-7.	Study design
75	Koplin, J. J.,Osborne, N. J.,Wake, M.,Martin, P. E.,Gurrin, L. C.,Robinson, M. N.,Tey, D.,Slaa, M.,Thiele, L.,Miles, L.,Anderson, D.,Tan, T.,Dang, T. D.,Hill, D. J.,Lowe, A. J.,Matheson, M. C.,Ponsonby, A. L.,Tang, M. L.,Dharmage, S. C.,Allen, K. J.. Can early introduction of egg prevent egg allergy in infants? A population-based study. J Allergy Clin Immunol. 2010;126:807-13.	Study design, Independent Variable
76	Koplin, J.,Dharmage, S. C.,Gurrin, L.,Osborne, N.,Tang, M. L.,Lowe, A. J.,Hosking, C.,Hill, D.,Allen, K. J.. Soy consumption is not a risk factor for peanut sensitization. J Allergy Clin Immunol. 2008;121:1455-9.	Study design, Independent Variable
77	Kramer, B.,Raczynska, J.,Kaczmarek, J.,Lukamowicz, J.,Pasowska, R.,Puchala, B.. Genetic and environmental conditions involved in assessment of the immunological state in children with atopic dermatitis. Rocz Akad Med Bialymst. 1995;40:439-47.	Study design, Independent Variable
78	Kramer, M. S.,Chalmers, B.,Hodnett, E. D.,Sevkovskaya, Z.,Dzikovich, I.,Shapiro, S.,Collet, J. P.,Vanilovich, I.,Mezen, I.,Ducruet, T.,Shishko, G.,Zubovich, V.,Mknuik, D.,Gluchanina, E.,Dombrovskiy, V.,Ustinovitch, A.,Kot, T.,Bogdanovich, N.,Ovchinikova, L.,Helsing, E.. Promotion of Breastfeeding Intervention Trial (PROBIT): a randomized trial in the Republic of Belarus. Jama. 2001;285:413-20.	Independent Variable
79	Kramer, M. S.,Moroz, B.. Do breast-feeding and delayed introduction of solid foods protect against subsequent atopic eczema?. J Pediatr. 1981;98:546-50.	Independent Variable
80	Krogulska, A.,Wąsowska-Królikowska, K.,Dynowski, J.. Usefulness of atopy patch tests with food allergens in diagnosis of food allergy in children with dermatitis atopica. Przeglad Pediatryczny. 2007;37:245-249.	Health Status, Independent Variable, Language
81	Kucukosmanoglu, E.,Yazi, D.,Yesil, O.,Akkoc, T.,Gezer, M.,Bakirci, N.,Bahceciler, N. N.,Barlan, I. B.. Prevalence of egg sensitization in Turkish infants based on skin prick test. Allergol Immunopathol (Madr). 2008;36:141-4.	Study design
82	Kummeling, I.,Thijs, C.,Huber, M.,van de Vijver, L. P.,Snijders, B. E.,Penders, J.,Stelma, F.,van Ree, R.,van den Brandt, P. A.,Dagnelie, P. C.. Consumption of organic foods and risk of atopic disease during the first 2 years of life in the Netherlands. Br J Nutr. 2008;99:598-605.	Study design
83	Laubereau, B.,Brockow, I.,Zirngibl, A.,Koletzko, S.,Gruebl, A.,von Berg, A.,Filipiak-Pittroff, B.,Berdel, D.,Bauer, C. P.,Reinhardt, D.,Heinrich, J.,Wichmann, H. E.. Effect of breast-feeding on the development of atopic dermatitis during the first 3 years of life--results from the GINI-birth cohort study. J Pediatr. 2004;144:602-7.	Independent Variable

	Citation	Reasons for Exclusion
84	Lee, J. M.,Neher, J. O.,Kelsberg, G.,Safranek, S.. Atopic Eczema and Early Introduction of Solid Foods. Am Fam Physician. 2015;92:523-4.	Study design
85	Levin, M.,Goga, A.,Doherty, T.,Coovadia, H.,Sanders, D.,Green, R. J.,Kling, S.. Allergy and infant feeding guidelines in the context of resource-constrained settings. J Allergy Clin Immunol. 2016.	Study design
86	Luoma, R.. Environmental allergens and morbidity in atopic and non-atopic families. Acta Paediatr Scand. 1984;73:448-53.	Independent Variable
87	Majeed, R.,Rajar, U. D.,Shaikh, N.,Majeed, F.,Arain, A. A.. Risk factors associated with childhood asthma. J Coll Physicians Surg Pak. 2008;18:299-302.	Independent Variable
88	Mauro-Martín, I. S.,Bodega-Villanueva, P.,Romero-Caamaño, E.,Micó-Moreno, V.,Garicano-Vilar, E.. Association between timing of food introduction in on first year old and the prevalence of allergies [spanish]. Revista Espanola de Nutricion Humana y Dietetica. 2014;18:145-154.	Language
89	Mavale-Manuel, S.,Alexandre, F.,Duarte, N.,Albuquerque, O.,Scheinmann, P.,Poisson-Salomon, A. S.,de Blic, J.. Risk factors for asthma among children in Maputo (Mozambique). Allergy. 2004;59:388-93.	Independent Variable
90	McKean, M.,Caughey, A. B.,Leong, R. E.,Wong, A.,Cabana, M. D.. The Timing of Infant Food Introduction in Families With a History of Atopy. Clin Pediatr (Phila). 2015;54:745-51.	Dependent Variable
91	Metcalfe, J. R.,D'Vaz, N.,Makrides, M.,Gold, M. S.,Quinn, P.,West, C. E.,Loh, R.,Prescott, S. L.,Palmer, D. J.. Elevated IL-5 and IL-13 responses to egg proteins predate the introduction of egg in solid foods in infants with eczema. Clin Exp Allergy. 2016;46:308-16.	Health Status, Dependent Variable
92	Midwinter, R. E.,Morris, A. F.,Colley, J. R.. Infant feeding and atopy. Arch Dis Child. 1987;62:965-7.	Study design, Independent Variable
93	Mihrshahi, S.,Webb, K.,Almqvist, C.,Kemp, A. S.. Adherence to allergy prevention recommendations in children with a family history of asthma. Pediatr Allergy Immunol. 2008;19:355-62.	Dependent Variable
94	Milner, J. D.,Stein, D. M.,McCarter, R.,Moon, R. Y.. Early infant multivitamin supplementation is associated with increased risk for food allergy and asthma. Pediatrics. 2004;114:27-32.	Independent Variable
95	Miyake, Y.,Yura, A.,Iki, M.. Breastfeeding and the prevalence of symptoms of allergic disorders in Japanese adolescents. Clin Exp Allergy. 2003;33:312-6.	Study design
96	Moore, W. J.,Midwinter, R. E.,Morris, A. F.,Colley, J. R.,Soothill, J. F.. Infant feeding and subsequent risk of atopic eczema. Arch Dis Child. 1985;60:722-6.	Independent Variable
97	Morgan, J. B.,Lucas, A.,Fewtrell, M. S.. Does weaning influence growth and health up to 18 months?. Archives of Disease in Childhood: Education and Practice Edition. 2004;89:728-733.	Study design

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98	Morin, K. H.. Food Allergies: New Evidence for Peanut Introduction. MCN Am J Matern Child Nurs. 2016;41:188.	Study design
99	Nakamura, Y.,Oki, I.,Tanihara, S.,Ojima, T.,Ito, Y.,Yamazaki, O.,Iwama, M.,Tabata, Y.,Katsuyama, K.,Sasai, Y.,Nakagawa, M.,Matsushita, A.,Hossaka, K.,Sato, J.,Hidaka, Y.,Uda, H.,Nakamata, K.,Yanagawa, H.. Relationship between breast milk feeding and atopic dermatitis in children. J Epidemiol. 2000;10:74-8.	Study design, Independent Variable
100		Language
101	Natsume, O.,Kabashima, S.,Nakasato, J.,Yamamoto-Hanada, K.,Narita, M.,Kondo, M.. Early introduction of egg for infants with atopic dermatitis to prevent egg allergy: A double-blind placebo-controlled randomized clinical trial[abstract only]. Journal of Allergy and Clinical Immunology. 2016;137.	Study design
102	Neild, V.. Diet and atopic eczema. Mod Midwife. 1994;4:22.	Study design
103	Nwaru, B. I.,Erkkola, M.,Ahonen, S.,Kaila, M.,Haapala, A. M.,Kronberg-Kippila, C.,Salmelin, R.,Veijola, R.,Ilonen, J.,Simell, O.,Knip, M.,Virtanen, S. M.. Age at the introduction of solid foods during the first year and allergic sensitization at age 5 years. Pediatrics. 2010;125:50-9.	Dependent Variable
104	Nwaru, B. I.,Takkinen, H. M.,Niemela, O.,Kaila, M.,Erkkola, M.,Ahonen, S.,Tuomi, H.,Haapala, A. M.,Kenward, M. G.,Pekkanen, J.,Lahesmaa, R.,Kere, J.,Simell, O.,Veijola, R.,Ilonen, J.,Hyoty, H.,Knip, M.,Virtanen, S. M.. Introduction of complementary foods in infancy and atopic sensitization at the age of 5 years: timing and food diversity in a Finnish birth cohort. Allergy. 2013;68:507-16.	Dependent Variable
105	Oddy, W. H.,Sherriff, J. L.. Breastfeeding, body mass index, asthma and atopy in children. Asia Pac J Public Health. 2003.	Independent Variable
106	Oddy, W. H.. Breastfeeding and asthma in children: findings from a West Australian study. Breastfeed Rev. 2000;8:5-11.	Independent Variable
107	Oehling, A.. Importance of food allergy in childhood asthma. Allergol Immunopathol (Madr). 1981:71-3.	Study design
108	Ogbuanu, I. U.,Karmaus, W.,Arshad, S. H.,Kurukulaaratchy, R. J.,Ewart, S.. Effect of breastfeeding duration on lung function at age 10 years: a prospective birth cohort study. Thorax. 2009;64:62-6.	Independent Variable
109	Ozmert, E. N.,Kale-Cekinmez, E.,Yurdakok, K.,Sekerel, B. E.. Determinants of allergic signs and symptoms in 24-48-month-old Turkish children. Turk J Pediatr. 2009;51:103-9.	Study design
110	Parihar, H.,Kumar, L.,Puri, R.,Kumar, V.. The incidence of allergic diseases and feeding patterns in children upto 2 years of age. Indian J Pediatr. 1984;51:7-12.	Study design
111	Paton, J.,Kljakovic, M.,Ciszek, K.,Ding, P.. Infant Feeding Practices and Nut Allergy over Time in Australian School Entrant Children. Int J Pediatr. 2012;2012:675724.	Study design, Age

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112	Pesonen, M.,Kallio, M. J.,Ranki, A.,Siimes, M. A.. Prolonged exclusive breastfeeding is associated with increased atopic dermatitis: a prospective follow-up study of unselected healthy newborns from birth to age 20 years. Clin Exp Allergy. 2006;36:1011-8.	Independent Variable
113	Peters, R. L.,Allen, K. J.,Dharmage, S. C.,Lodge, C. J.,Koplin, J. J.,Ponsonby, A. L.,Wake, M.,Lowe, A. J.,Tang, M. L.,Matheson, M. C.,Gurrin, L. C.. Differential factors associated with challenge-proven food allergy phenotypes in a population cohort of infants: a latent class analysis. Clin Exp Allergy. 2015;45:953-63.	Study design
114	Peters, T. J.,Golding, J.. The epidemiology of childhood eczema: II. Statistical analyses to identify independent early predictors. Paediatr Perinat Epidemiol. 1987;1:80-94.	Independent Variable
115	Pitt, Tj,Watson, W.,Ferguson, A.,Dimich-Ward, H.,Dybuncio, A.,Kozyrskyj, Al. Delay In The Introduction Of Allergenic Foods Is Not Associated With An Increased Risk For Sensitization In A High Risk Cohort [Abstract]. Journal of allergy and clinical immunology. 2010;125.	Study design
116	Pohl, C. A.. Timing of cereal introduction to the infant diet. Patient Care for the Nurse Practitioner. 2006;9.	Study design
117	Pohlabeln, H.. Effect modification by familial predisposition when analyzing the influence of breastfeeding and pet keeping on the development of allergic diseases in children [german]. Allergologie. 2012;35:44-53.	Language
118	Poongadan, M. N.,Gupta, N.,Kumar, R.. Dietary pattern and asthma in India. Pneumonol Alergol Pol. 2016;84:160-7.	Age
119	Poysa, L.,Pulkkinen, A.,Korppi, M.,Remes, K.,Juntunen-Backman, K.. Diet in infancy and bronchial hyperreactivity later in childhood. Pediatr Pulmonol. 1992;13:215-21.	Independent Variable
120	Poysa, L.. Atopy in children with and without a family history of atopy. II. Skin reactivity. Acta Paediatr Scand. 1989;78:902-6.	Independent Variable
121	Prasad, S.,Rana, R. K.,Sheth, R.,Mauskar, A. V.. A Hospital Based Study to Establish the Correlation between Recurrent Wheeze and Vitamin D Deficiency Among Children of Age Group Less than 3 Years in Indian Scenario. J Clin Diagn Res. 2016;10.	Independent Variable, Dependent Variable
122	Pratt, H. F.. Breastfeeding and eczema. Early Hum Dev. 1984;9:283-90.	Independent Variable
123	Pugh, R. J.. Infant feeding in perspective. Practitioner. 1982;226:1917-25.	Study design
124	Quah, P. L.,Loo, E. X.,Lee, G. N.,Kuo, I. C.,Gerez, I.,Llanora, G. V.,Chan, Y. H.,Aw, M.,Shek, L. P.,Lee, B. W.. Clinical phenotype and allergen sensitization in the first 2 years as predictors of atopic disorders at age 5 years. World Allergy Organ J. 2015;8:33.	Independent Variable
125	Rosenberg, K.. Early Introduction Reduces Risk of Some Food Allergies. Am J Nurs. 2017;117:65-66.	Study design

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126	Roslan, K.,Szczepanski, M.,Kaczmarski, M.,Zapolska, B.,Uscinowicz, M.,Wasilewska, J.,Solarz, E.. Environmental and constitutional conditions and food hypersensitivity in children. Rocz Akad Med Bialymst. 1995;40:448-51.	Study design, Health Status
127	Satwani, H.,Rehman, A.,Ashraf, S.,Hassan, A.. Is serum total IgE levels a good predictor of allergies in children?. J Pak Med Assoc. 2009;59:698-702.	Study design
128	Sausenthaler, S.,Heinrich, J.,Koletzko, S.. Early diet and the risk of allergy: What can we learn from the prospective birth cohort studies GINIplus and LISAplus?. American Journal of Clinical Nutrition. 2011;94.	Study design
129	Sherriff, A.,Peters, T. J.,Henderson, J.,Strachan, D.. Risk factor associations with wheezing patterns in children followed longitudinally from birth to 3(1/2) years. Int J Epidemiol. 2001;30:1473-84.	Independent Variable
130	Shohet, L.,Shahar, E.,Davidson, S.. Breast feeding as prophylaxis for atopic eczema: a controlled study of 368 cases. Acta Paediatr Hung. 1985;26:35-9.	Independent Variable
131	Siltanen, M.,Kajosaari, M.,Poussa, T.,Saarinen, K. M.,Savilahti, E.. A dual long-term effect of breastfeeding on atopy in relation to heredity in children at 4 years of age. Allergy. 2003;58:524-30.	Independent Variable
132	Silvers, K. M.,Frampton, C. M.,Wickens, K.,Pattemore, P. K.,Ingham, T.,Fishwick, D.,Crane, J.,Town, G. I.,Epton, M. J.. Breastfeeding protects against current asthma up to 6 years of age. J Pediatr. 2012;160.	Independent Variable
133	Smith, P.. Dietary prevention of food allergies in infants. Australian Journal of Pharmacy. 2012;93:80-83.	Study design
134	Sybilski, A. J.,Doboszyńska, A.,Samoliński, B.. Influence of selected risk factors on the development of allergy during the first year of life [polish]. Przeglad Pediatryczny. 2008;38:13-19.	Independent Variable, Language
135	Ta, V.,Laubach, S.. Introduction of complementary foods and the relationship to food allergy. Pediatrics. 2014.	Study design
136	Taitz, L.. Feeding children in the first year of life. Community Nurse. 1990;26:81-84.	Study design
137	Takemura, Y.,Sakurai, Y.,Honjo, S.,Kusakari, A.,Hara, T.,Gibo, M.,Tokimatsu, A.,Kugai, N.. Relation between breastfeeding and the prevalence of asthma : the Tokorozawa Childhood Asthma and Pollinosis Study. Am J Epidemiol. 2001;154:115-9.	Independent Variable
138	Tan, Jw- L.,Valerio, C.,Barnes, E. H.,Asperen, P. P.,Kakakios, A. M.,Campbell, D. E.. Early introduction of dietary egg reduces egg sensitization at 12 months of age in infants at risk of allergic disease [abstract only]. Journal of Allergy and Clinical Immunology. 2016;137.	Study design
139	Taylor, B.. Infant feeding and allergy: fact and fiction. Midwife Health Visit Community Nurse. 1984;20:354-60.	Study design
140	Tromp,, II,Briede, S.,Kiefte-de Jong, J. C.,Renders, C. M.,Jaddoe, V. W.,Franco, O. H.,Hofman, A.,Raat, H.,Moll, H. A.. Factors associated with the timing of introduction of complementary feeding: the Generation R Study. Eur J Clin Nutr. 2013;67:625-30.	Dependent Variable

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141	van Odijk, J.,Hulthen, L.,Ahlstedt, S.,Borres, M. P.. Introduction of food during the infant's first year: a study with emphasis on introduction of gluten and of egg, fish and peanut in allergy-risk families. Acta Paediatr. 2004;93:464-70.	Study design, Dependent Variable
142	Ventura, A.,De Seta, L.,Martelossi, S.,Florean, P.,Maggiore, G.,Salvatore, C. M.,Berzioli, M.,Guidobaldi, G.,Lorenzini, G.,Peressini, P.,Pesenti, P.,Rollo, G.,Sacher, B.,Santoro, L.,Stanzione, V.,Stranamore, D.,Zannerio, E.. Soy allergy and DSCG in atopic eczema: "much ado about nothing"?. Pediatr Med Chir. 1996;18:283-8.	Health Status, Independent Variable
143	Verduci, E.,Banderali, G.,Peroni, D.,Lassandro, C.,Radaelli, G.. Duration of exclusive breastfeeding and wheezing in the first year of life: A longitudinal study. Allergol Immunopathol (Madr). 2016.	Independent Variable
144	Visser, H. K.. Dietary influences on infection and allergy in infants: introduction. J Nutr. 2008;138.	Study design
145	Waddell, L.. Introduction of solids in babies at risk of allergies. J Fam Health Care. 2014;24:22-7.	Study design
146	Waidyatillake, N. T.,Simpson, J. A.,Allen, K. J.,Lodge, C. J.,Dharmage, S. C.,Abramson, M. J.,De Livera, A. M.,Matheson, M. C.,Erbas, B.,Hill, D. J.,Lowe, A. J.. The effect of breastfeeding on lung function at 12 and 18 years: A prospective cohort study. European Respiratory Journal. 2016;48:125-132.	Independent Variable
147	Wegienka, G.,Ownby, D. R.,Havstad, S.,Williams, L. K.,Johnson, C. C.. Breastfeeding history and childhood allergic status in a prospective birth cohort. Ann Allergy Asthma Immunol. 2006;97:78-83.	Independent Variable
148	West, C. E.,Hammarstrom, M. L.,Hernell, O.. Probiotics during weaning reduce the incidence of eczema. Pediatr Allergy Immunol. 2009;20:430-7.	Independent Variable
149	White, J. M.,McFadden, J. P.. Contact allergens in food ingredients and additives: atopy and the hapten-atopy hypothesis. Contact Dermatitis. 2008;58:245-6.	Study design, Dependent Variable
150	Woicka-Kolejwa, K.,Zaczeniuk, M.,Majak, P.,Pawlowska-Iwanicka, K.,Kopka, M.,Stelmach, W.,Jerzynska, J.,Stelmach, I.. Food allergy is associated with recurrent respiratory tract infections during childhood. Postepy Dermatol Alergol. 2016;33:109-13.	Study design, Dependent Variable
151	Woś, H.,Cholewa, Z.,Brozek, G.. The influence of breast-feeding on the rate of occurrence of bronchial asthma in children at the younger school age. Pediatria Wspolczesna. 2003;5:21-27.	Independent Variable, Language
152	Wright, A. L.,Holberg, C. J.,Martinez, F. D.,Halonen, M.,Morgan, W.,Taussig, L. M.. Epidemiology of physician-diagnosed allergic rhinitis in childhood. Pediatrics. 1994;94:895-901.	Dependent Variable
153	Wright, A. L.,Holberg, C. J.,Taussig, L. M.,Martinez, F. D.. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. Thorax. 2001;56:192-7.	Independent Variable
154	Wright, A. L.,Holberg, C. J.,Taussig, L. M.,Martinez, F.. Maternal asthma status alters relation of infant feeding to asthma in childhood [not peer rev jl). Adv Exp Med Biol. 2000;478:131-7.	Study design

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155	Xu, M.,Wang, Y.,Dai, Z.,Zhang, Y.,Li, Y.,Wang, J.. Comparison of growth and nutritional status in infants receiving goat milk-based formula and cow milk-based formula: A randomized, double-blind study. Food and Nutrition Research. 2015;59.	Independent Variable, Dependent Variable
156	Yamakawa, M.,Yorifuji, T.,Kato, T.,Yamauchi, Y.,Doi, H.. Breast-feeding and hospitalization for asthma in early childhood: a nationwide longitudinal survey in Japan. Public Health Nutr. 2015;18:1756-61.	Independent Variable
157	Young, H. B.,Buckley, A. E.,Hamza, B.,Mandarano, C.. Milk and lactation: some social and developmental correlates among 1,000 infants. Pediatrics. 1982;69:169-75.	Study design, Independent Variable
158	Zeiger, R. S.,Heller, S.,Mellon, M. H.,Forsythe, A. B.,O'Connor, R. D.,Hamburger, R. N.,Schatz, M.. Effect of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: a randomized study. J Allergy Clin Immunol. 1989;84:72-89.	Independent Variable