Associations between diet diversity during infancy and atopic disease in later life: Systematic review

YuXin Lv, MMeD,[a] Lin Chen, MMeD,[a] Heping Fang, MMeD,[a] and Yan Hu, MD, PhD[b] *Chongqing and Beijing, China*

Background: The incidence of allergic disease remains high, and many studies have focused on the association between food diversity in infancy and allergic disease later in life, but their conclusions are still controversial.
Objective: We aimed to synthesize the literature on the association between childhood diet diversity and atopic disease.
Methods: We searched the PubMed, Cochrane Library, Embase, Scopus, VPCS, and Wanfang databases for studies about food diversity and atopic disease. Seventeen high-quality studies, 14 cohort studies, and 1 case–control study were included from 5244 studies with sample sizes ranging from 100 to 5225.
Results: All high-quality cohort studies showed that increasing food diversity in infancy can effectively prevent the occurrence of food allergies (5/5). Moderate evidence showed that increased food diversity reduced the risk of asthma (4/6), food sensitization (3/5), and atopic dermatitis (3/5). However, its effect on eczema (5), allergic rhinitis (4), and other diseases remains controversial.
Conclusions: Increasing food diversity during infancy is a potential method for preventing food allergy, asthma, atopic dermatitis, and food sensitization later in life. There is little or no comparative evidence about the protective effect of food diversity on other atopic diseases. (J Allergy Clin Immunol Global 2024;3:100221.)

Key words: *Allergy, complementary food, atopic disease, infant*

Abbreviations used
AD: Atopic dermatitis
ORs: Odds ratios

The incidence of allergic disease is increasing yearly. Once diagnosed, most allergic diseases seriously affect the quality of life of individuals and families[1] and cause a great economic burden to families and society.[2] To date, the treatment options for allergic disease are limited. Treatment often involves drugs aimed at different allergic symptoms[3] or allergen-specific immunotherapy for children with severe and persistent symptoms that seriously affect their quality of life.[4] However, as a result of the public's fear of hormones, children have poor compliance with treatment, resulting in repeated symptoms; however, even with allergen-specific immunotherapy, it is unlikely that children will develop tolerance in the short term.[4] Therefore, early prevention of allergic disease is crucial.

Allergic disease prevention strategies have changed substantially over the past few decades, especially concerning the introduction of solid foods in infancy. Based on the results of the Learning Early About Peanut (LEAP), LEAP-On, and Enquiring About Tolerance (EAT) studies published in the *New England Journal* in 2017, the National Institute of Allergy and Infectious Disease (NIAID) in the United States[5] and the Australasian Society of Clinical Immunology and Allergy (ASCIA) in Australia[6] successively published guidelines for the prevention of peanut allergy. Routine early introduction of peanut in children at high allergy risk (those with severe eczema and/or egg allergy) and even in low-risk children (4-6 months of age) is encouraged. In addition to the time of introduction of complementary foods,[7,8] increasing attention has been given to the influence of the type and quantity of complementary foods on allergic disease. The 2020 European Society of Allergy and Clinical Immunology (EAACI) position paper suggests that the risk of later allergy can be reduced by increasing food diversity in infancy and early childhood.[9] Unfortunately, this recommendation is based on the principle of harmlessness rather than obvious protective effects. In addition, the definition of food diversity and its impact on allergic disease reported in the literature is in dispute.

In this systematic review, we focus on the association between the diversity of complementary foods in infants and the occurrence of later atopic disease, hoping to provide a basis for clinical guidance on complementary infant foods to prevent atopic disease.

METHODS

This systematic review protocol was registered in the International Prospective Register of Systematic Reviews (Prospero; CRD42022303382) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist.

From the [a]National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Pediatrics, Children's Hospital of Chongqing Medical University, Chongqing; and [b]Children's Health care Center, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing.

Received for publication April 30, 2023; revised July 21, 2023; accepted for publication August 21, 2023.
Available online January 28, 2024.

Corresponding author: Yan Hu, MD, PhD, Children's Health care Center, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China. E-mail: hy420@126.com.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

2772-8293

https://doi.org/10.1016/j.jacig.2024.100221

Search strategy

The PubMed, Cochrane Library, Embase, Scopus, Wanfang Medical (g.wanfangdata.com.cn), and VIP (www.cqvip.com) databases were searched from database inception to February 26, 2023. The results were limited to studies in English and Chinese. The search strategy was developed for searching PubMed, then adapted for the other databases. The complete search terms and strategies used are listed in this article's Online Repository at www.jaci-global.org. Additional references were included by searching the references cited in the retrieved studies.

Inclusion criteria

Studies that examined the association between diet diversity during infancy and atopic conditions (asthma, eczema, food allergy, food sensitization, inhalation sensitization, allergic rhinitis, atopic dermatitis [AD], and wheezing) were included. Study designs included cohort studies and case–control studies. Study outcomes included the occurrence of the above atopic disease in children. The main diagnostic criterion was atopic disease diagnosed by a doctor.

Exclusion criteria

We excluded reviews, discussions, letters, editorials, animal experiments, and studies targeting adults. Studies on the effects of single food group diversity (such as vegetable/fruit/meat/dairy product diversity) on allergic outcomes in children were also excluded.

Study selection

Two reviewers initially screened the title, abstract, and keywords of every record identified with the search strategy, and they retrieved the full texts of potentially relevant trials and of records for which the relevance was unclear. The same reviewers independently applied the inclusion criteria to each potentially relevant trial to determine its eligibility. Any discrepancy was discussed and resolved through consensus.

Quality assessment strategy

Two review authors (Y.L., L.C.) independently assessed the risk of bias for each study using the Newcastle-Ottawa Scale for quality assessment of nonrandomized studies.[10]

For the Newcastle-Ottawa Scale, a score of at least 6 out of 9 indicated high quality. The item assessing the adequacy of follow-up was 90%. We resolved any disagreement by discussion or by involving a senior assessor (Y.H.).

Data extraction, analysis, and synthesis

One reviewer (Y.X.L.) extracted the data from the included studies, and the second reviewer (C.L.) checked the extracted data. If differences in opinion existed, they were resolved by discussion or by a senior reviewer (Y.H.).

Data were extracted from each article and compiled for each atopic disease. We reported odds ratios (ORs) with 95% confidence intervals (CIs) and, where available, *P* values for association with food diversity as reported by the original article.

A narrative synthesis of the findings was performed because most data were not similar enough with regard to outcome selection, definitions, and time settings to perform the data synthesis needed for a meta-analysis.

RESULTS

A total of 5244 related studies were retrieved by searching the databases and tracing references. After title, abstract, and full text screening and rescreening according to inclusion and exclusion criteria, we finally included 14 articles based on 13 cohort studies and 1 case–control study for analysis (Fig 1 and Table I). The sample sizes at baseline ranged from 100 to 5225, and the follow-up time ranged from 1 to 15 years. Among them, 1 study included the effect of food diversity on atopic disease via a retrospective survey. Most studies were from Europe (n = 12), with the remaining studies from Asia (n = 2) and New Zealand (n = 1). All studies' data sources, inclusion and exclusion criteria, and outcome indicators were clear. Ten of the 15 articles did not contain the original data and the combined effect size could not be counted, so here, we conducted only a qualitative analysis.

Quality of evidence assessment

Tables II and III show quality assessments of the included studies. According to Newcastle-Ottawa Scale evaluation of the cohort studies, the included studies were all high-quality studies, with an average score of 8.1. Of the 15 included studies, all 15 described the definition of food diversity or diet quality scores, 6 reported loss to follow-up rates of approximately 10% to 33%, 3 studies were biased in the selection of exposure cohorts, and 1 study included subjects with preexisting allergic disease.

Airway-related allergic disease

A total of 7 articles reported the effect of food diversity in infancy on later airway-related allergic disease, including 6 studies involving asthma, 4 involving allergic rhinitis, 4 involving inhalation sensitization, and 1 involving wheezing. Four studies suggested that food diversity had a preventive effect on asthma, although there was insufficient supporting evidence for preventing other airway-related allergic disease.

Asthma. A total of 6 studies on the relationship between the diversity of complementary foods and later asthma were included. Four studies showed an inverse association between early food diversity and asthma development. Roduit et al[11] pointed out that in the first year of life, the incidence of asthma was significantly reduced by 26% for each additional food (OR = 0.74; 95% CI, 0.61-0.89). Nwaru et al[12] found that insufficient food diversity at 12 months was associated with an increased risk of asthma (OR = 4.19; 95% CI, 2.31-7.58). Stampfli et al[13] found that in the second year after birth, each additional food was associated with a reduced risk of asthma by 25% (OR = 0.75; 95% CI, 0.58-0.98). Zhong et al[14] showed that after adjusting for food allergy history and other potential confounding factors, food diversity at 12 months showed a significant dose–response–negative correlation with respiratory tract allergic disease—that is, people with insufficient food diversity had an increased risk of developing asthma (OR = 2.69; 95% CI, 1.22-5.59). Two other studies did not observe a clear association between food diversity in infancy and asthma. Markevych et al[15] were unable to explain the

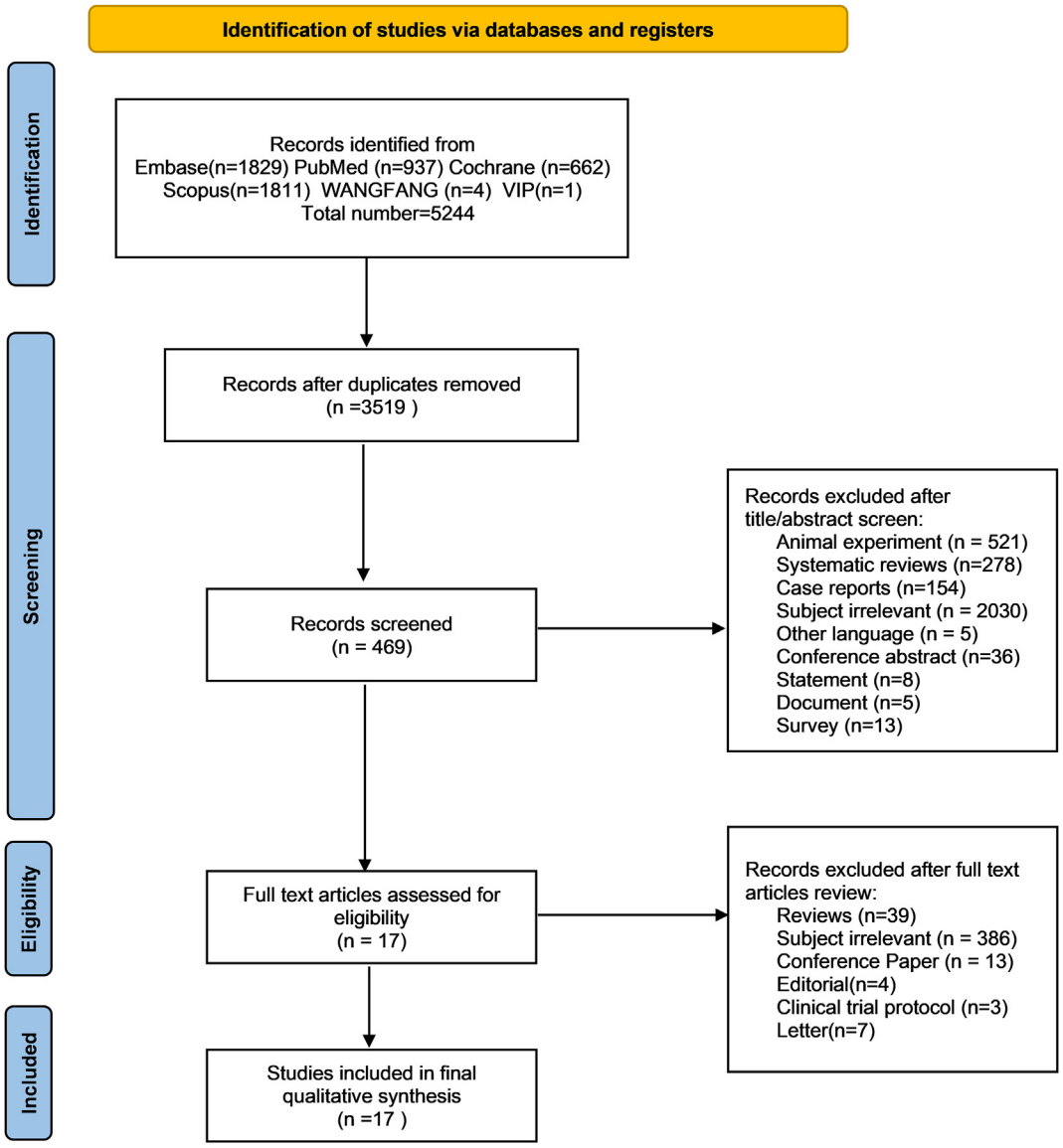

FIG 1. Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) diagram for study identification, screening, selection, and inclusion.

relationship between food diversity and asthma; Zutavern et al[16] did not find a significant association between food diversity and asthma at 4 months of age ($P > .05$).

Allergic rhinitis. A total of 4 studies on the relationship between the diversity of complementary foods and later allergic rhinitis were included. Only Nwaru et al[12] reported that an insufficient variety of complementary foods in infants at 12 months of age increased the risk of allergic rhinitis (OR = 3.10; 95% CI, 1.66-5.78). None of the remaining 3 studies found a significant association between food diversity and allergic rhinitis. Roduit et al[11] found that there was a negative correlation between food diversity and allergic rhinitis, but the difference was not statistically significant ($P > .05$). Markevych et al[15] used different classification methods for food diversity and were unable to reach a consistent conclusion. The study of Zutavern et al[16] did not find a significant correlation between food diversity at 4 months of age and allergic rhinitis ($P > .05$).

Inhalation allergen sensitization. A total of 4 studies on the relationship between the diversity of complementary foods and inhalation allergen sensitization in infants and young children were included. Markevych et al[15] found that higher food diversity within 1 year of age in infants with skin symptoms was associated with a reduced risk of inhalation allergen sensitization (OR = 0.88; 95% CI, 0.80-0.95). Nwaru et al[17] found that at 6 months, introduction of ≤4 food items was adversely associated with most of the end points of inhalation allergen sensitization (OR = 1.88; 95% CI, 1.26-2.79). The remaining 3 studies had no clear evidence to suggest an association between inhalation allergen sensitization and food diversity. Roduit et al[11] reported a negative correlation trend between food variety and inhalation allergen sensitization, but there was no statistically significant difference ($P > .05$). Zutavern et al[16] did not find a significant correlation between food diversity and inhalation allergen sensitization at 4 months of age ($P > .05$).

TABLE I. Characteristics of included studies

Reference no.	Study site, name, cohort (sample size)	Allergy outcomes	Outcome age (years)	Definition of diet diversity (no. of subjects)	Exposure	Limitations	Conclusion
11	Europe, PASTURE/ EFRAIM, birth cohort (856)	Asthma, allergic rhinitis, FA, food sensitization, inhalant sensitization	6	Total count of no. of different food groups (6)	Monthly diet diary between 3 and 12 months	Reverse causality cannot be completely excluded; selected rural study population	Increased diversity of food within first year of life might have protective effect on asthma, FA, and food sensitization
12	Finland, DIPP, birth cohort (3142)	Asthma, wheeze, allergic rhinitis, eczema	5	Total count of no. of different food groups	Age-specific dietary questionnaires at 3, 6, and 12 months	Selected participants carrying genetic risk for type 1 diabetes	Less food diversity during first year of life might increase risk of asthma and allergies in childhood
13	Europe, PASTURE, birth cohort (1014)	Asthma, FA, AD	6	Total count of no. of different food groups (11)	Questionnaires at 1.5 and 2 years	Selected rural study population	Increased food diversity in second year of life is inversely associated with development of asthma, and consumption of dairy products might have protective effect on allergic disease
14	China, Tongji Maternal and Child Health Cohort (2251)	Asthma, eczema, allergic rhinitis, wheeze, allergic cough, urticaria, or other contact dermatitis	2	Total count of no. of different food groups (n = 6 at 6 months; n = 11 at 12 months)	Telephone interview at 1, 3, 6, and 12 months	Potential information bias	More diverse diet within first year of life was associated with reduced risk of allergic disease at 1 to 2 years of age
15	Germany, LISAplus, birth cohort (2518)	Asthma, allergic rhinitis, food sensitization, inhalant sensitization, eczema	15	Total count of no. of different food groups (8); total count of no. of different food items (48)	Parent questionnaires at 6 months and 1 year	Some participants had allergy outcomes before study	Higher food diversity during first year of life appears to decrease risk of allergic sensitization to aeroallergens up to 15 years only among children with early skin symptoms in German birth cohort
16	Germany, LISA, birth cohort (2073)	Asthma, allergic rhinitis, food sensitization, inhalant sensitization, eczema	6	Total count of no. of different food groups (8)	Questionnaires at 4 months	High ratio of loss to follow-up	Greater diversity of solid food items introduced until 4 months of age was risk factor for eczema in children without early skin or allergic symptoms and less diverse diet within first 4 months were statistically significantly positively associated with food sensitization
17	Finland, DIPP, birth cohort (3781)	Food sensitization, inhalant sensitization	5	Total count of no. of different food groups	Age-specific dietary questionnaires at 3, 6, and 12 months	Selected participants with genetic risk for type 1 diabetes	Less food diversity already at 3 months of age may increase risk of atopic sensitization
18	Germany, high-risk cohort (4753)	Eczema	4	Total count of no. of different food groups (8)	Questionnaires at 1 year	Selection bias due to loss to follow-up; misclassification due to recall bias	No significant association between food diversity and eczema exists

(Continued)

TABLE I. *(Continued)*

Reference no.	Study site, name, cohort (sample size)	Allergy outcomes	Outcome age (years)	Definition of diet diversity (no. of subjects)	Exposure	Limitations	Conclusion
19	New, Zealand Christchurch Birth cohort (1141)	Eczema	10	Total count of no. of different food items	Interview at 4 months	Selection bias due to loss to follow-up	Early exposure to diverse solid-food diet may increase risks of eczema in children susceptible to this condition
20	Europe, PASTURE, birth cohort (1041)	AD	4	Total count of no. of different food groups (6)	Monthly diet diary between 3 and 12 months	Selected rural study population	As early-life exposure, introduction of yogurt and diversity of food introduced in first year of life might have protective effects against AD
21	Italy, case–control study (902)	AD	<2	Total no. of food items or food groups included vegetables, legumes, or roots (potatoes, carrots, tomatoes, and beans), fruit (apples/pears, peaches/apricots/ plums, citrus fruits, and red fruits), cereals (maize/tapioca, rice, pasta, and gluten-free pasta), meat (poultry, pork, and beef), dairy products (cheese, and other dairy), fish, eggs, and nuts/cacao/ chocolate	Questionnaires at 4 and 5 months	Not mentioned	Introduction of high no. of different solid foods reduced risk of AD
22	Germany, atopy family history cohort (2252)	AD	1	Total count of no. of different food items	Weekly dietary diary by mother until 24 weeks	Retrospective study; selected participants with family history of AD	AD preventive effect in breast-fed infants is result of reduced diversity of solid foods fed during nursing period
23	England, FAIR Birth Cohort (969)	FA	10	Total count of no. of different food groups (7) measured by World Health Organization; total count of no. of different foods; fruit and vegetable diet diversity: 5 fruit and vegetable items (noncitrus fruits, citrus fruits, strawberry, vegetables not including potato and tomato, tomato); food allergen diversity assessing 8 main allergens (milk, egg, wheat, fish, soy, peanut, tree nuts, sesame)	Standardized questionnaire at 3, 6, 9, and 12 months	Data collected on maternal atopy and child eczema reported rather than diagnosed; selection bias due to loss to follow-up	Increased infant diet diversity, as measured by 4 different methods, decreased likelihood of developing FA

(Continued)

TABLE I. *(Continued)*

Reference no.	Study site, name, cohort (sample size)	Allergy outcomes	Outcome age (years)	Definition of diet diversity (no. of subjects)	Exposure	Limitations	Conclusion
24	Korea prospective birth cohort study (100)	FA	1	Total count of no. of different food groups (10)	Monthly questionnaires from 3 to 12 months	Results cannot be generalized to types of FA other than eggs; small sample size; no long-term follow-up	Greater food diversity within first 6 months of life may increase gut microbial diversity and reduce development of IgE-mediated HEA during infancy
25	England, FAIR Birth Cohort (969)	Food sensitization	10	No. of different foods or food groups consumed over given reference period; 21 foods: fruits (citrus fruit, noncitrus fruit, strawberries, tomato), vegetables, potato, pulses, nonwheat cereals (rice, oats), meat (chicken/turkey, lamb, beef, pork), and food allergens (cows' milk products, egg, wheat, peanut, tree nuts, fish, soy, and sesame)	Standardized questionnaire at ages 3, 6, and 9 months	Data collected on maternal atopy and child eczema reported rather than diagnosed; selection bias due to loss to follow-up	Reduced risk of food sensitization up to 2 years of age in those consuming higher diversity of foods in first 6-9 months of life

FA, Food allergy.

Wheezing. Nwaru et al[12] showed that decreased food diversity in infancy was associated with an increased risk of wheezing after 12 months of follow-up (OR = 2.49; 95% CI, 1.47-4.24).

Skin-related allergic disease

Ten related articles were included, including 5 for eczema and 5 for AD. Three studies suggested that food diversity had a preventive effect on AD, and the remaining 2 did not draw conclusions; however, there were inconsistencies in the effect of food diversity on eczema, and no conclusion could be drawn.

Eczema. A total of 5 studies on the relationship between the diversity of complementary foods and eczema in infants and young children were included. Only Markevych et al[15] found that those with high food diversity at 12 months of age had lower cumulative odds of developing eczema at age 15 (OR = 0.67; 95% CI, 0.48-0.94), but after correction for skin symptom type, there was no significant relationship between the two ($P > .05$).[15] Two other studies did not find a clear link between food diversity and eczema risk. Nwaru et al[12] showed that insufficient food diversity at 12 months was not significantly associated with the occurrence of eczema at 5 years of age ($P > .05$). Filipiak et al[18] reported that food diversity was not associated with the occurrence of eczema at 4 years old ($P > .05$). In addition, 2 studies suggested that early introduction to a variety of foods may lead to an increased risk of developing eczema in children. Fergusson et al[19] reported that at 10-year follow-up, children who were introduced to ≥4 foods at 4 months had 2.5 times the cumulative odds of developing eczema than those who were introduced to <4 foods ($P < .01$). Zutavern et al[16] found that food diversity introduced at <4 months of age was a risk factor for eczema in children without early skin/allergic symptoms (OR = 2.72; 95% CI, 1.24-5.99).

AD. A total of 5 studies on the relationship between the diversity of complementary foods and later AD were included. Three studies suggested that food variety had a protective effect on AD. Zhong et al[14] found that at 6 months, the risk of developing skin-related atopic disease was increased in the group without complementary food compared to the group with high food diversity (OR = 3.17; 95% CI, 1.23-8.15). Roduit et al[20] showed that the diversity of food at 1 year was associated with a reduced risk of AD after 1 year old, and each additional major food introduced was associated with a 24% lower probability of AD (OR = 0.76; 95% CI, 0.65-0.88). Turati et al[21] found that compared to no solid food intake, the ORs of the risk of AD for children introduced to a high number of different solid foods at 4 and 5 months were, respectively, 0.30 (95% CI, 0.11-0.81) and 0.44 (95% CI, 0.21-0.91). However, Stampfli et al[13] found that food diversity was negatively correlated with AD in the second year, but after adjusting for confounding factors such as AD history at 1 year old, no significant association was found ($P > .05$). Schoetzau et al[22] did not find a significant association between infant food diversity and AD at 24 weeks ($P > .05$).

Food allergies and food sensitization

A total of 9 articles on food allergy and sensitization were included, including 5 articles on food allergy and 5 articles on food sensitization. All 5 studies suggested that food diversity had a preventive effect on food allergy; 3 studies suggested that food diversity had a preventive effect on food sensitization; and the remaining 2 studies did not conclude that the two are related.

TABLE II. Results of quality assessment by Newcastle-Ottawa Scale for cohort studies

	Selection				Comparability	Outcome			
Reference	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Score
11	*	*	*	*	**	*	*	*	9
12	—	*	*	*	**	*	*	*	8
13	*	*	*	*	**	*	*	—	8
14	*	*	*	*	**	*	—	*	8
15	*	*	*	—	**	*	*	*	8
16	*	*	*	*	**	*	*	—	8
17	—	*	*	*	**	*	*	*	8
18	*	*	*	*	**	*	*	—	8
19	*	*	*	*	**	*	*	—	8
20	*	*	*	*	**	*	*	*	9
22	—	*	*	*	**	*	*	*	9
23	*	*	*	*	**	*	*	—	8
24	—	*	*	*	**	*	*	—	7
25	*	*	*	*	**	*	*	—	8

Study can be awarded maximum of 1 star for each numbered item within Selection and Exposure categories; maximum of 2 stars can be given for Comparability.

TABLE III. Results of quality assessment using Newcastle-Ottawa Scale for case–control studies

	Selection				Comparability	Outcome			
Reference	Is case definition adequate?	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cases and controls on the basis of design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Nonresponse rate	Scores
21	*	*	*	*	*	*	*	*	8

Study can be awarded maximum of 1 star for each numbered item within Selection and Exposure categories; maximum of 2 stars can be given for Comparability.

Food allergy. Of the 5 included studies, all 5 showed that food diversity in infancy could reduce the risk of food allergy. Roduit et al[11] found that children with low food diversity scores at 6 years had a higher risk of food allergy (OR = 0.70; 95% CI, 0.57-0.86). Stampfli et al[13] showed that there is a negative correlation between food diversity and the risk of food allergies in the second year of life (OR = 0.67; 95% CI, 0.50-0.90). Venter et al[23] found that food diversity at 6 months showed a reduced odds of developing food allergy at 1 year, 3 years, 10 years and over the first 10 years of life but not at 2 years, and that food diversity at 9 months could reduce the risk of food allergy over the first 10 years of life but not at 1 year of age old ($P = .0392$). Although Zhong et al[14] did not draw a significant conclusion at 6 months ($P > .05$), they showed that low food diversity at 12 months increased the risk of food allergy (OR = 2.78; 95% CI, 1.80-4.32). Lee et al[24] found that children with high diet diversity scores at 3 and 4 months of age were less likely to develop egg allergy in the high-risk group (OR = 0.02; 95% CI, 0-0.51/0.56) while there is no association of diet diversity at 6 to 12 months with the development of egg allergy ($P > .05$).

Food sensitization. A total of 5 studies on the relationship between the diversity of complementary foods and food sensitization were included. Roduit et al[11] showed that compared to children with high food diversity, children with low food diversity scores had a higher risk of food sensitization at 6 years old (OR = 0.72; 95% CI, 0.57-0.90). Nwaru et al[17] found that at 6 months, introduction of ≤4 food items was adversely associated with most of the end points of food sensitization (OR = 1.46; 95% CI, 0.98-2.19). Maslin et al[25] found that a higher diet diversity at 9 months decreased the odds of food sensitization at 2 years old (OR = 0.81; 95% CI, 0.67-0.98) and 3 years old (OR = 0.83; 95% CI, 0.7-0.98). Three other studies found no clear association between food diversity and food sensitization. Markevych et al[15] found inconsistent results resulting from the use of different food diversity classification methods, so they could not draw a conclusion. However, Zutavern et al[16] found that lower food diversity at 4 months old was positively correlated with food sensitization (OR = 0.49; 95% CI, 0.24-0.98).

DISCUSSION

A total of 5244 related studies were retrieved, and 15 high-quality cohort studies were finally included for systematic review. The results show that increasing the variety of complementary foods in infancy can effectively prevent food allergy (5/5); moderate evidence shows that increasing food variety can reduce the risk of asthma (4/6), AD (3/5), and food sensitization (3/5). However, the conclusions about its impact on eczema, allergic rhinitis, and other diseases are still controversial.

TABLE IV. Food diversity grouping methods

Study	Introduced complementary food	Exposure grouping measure	
		Exposure time	Diversity groups
11	(1) With major food items introduced in first year of life (n = 6, including vegetables or fruits, cereals, bread, meat, cake, and yogurt); (2) with same major food items but introduced in first 6 months of life; and (3) with all food items introduced in first year of life (n = 15, including any cow's milk, yogurt, other milk product, eggs, nuts, vegetables or fruits, cereals, bread, meat, fish, soy, margarine, butter, cake, and chocolate)	12 months	0-3 4-5 6 Continuous scores
12	Cow's milk and formula (as combined variable); potatoes; carrots; turnip; fruits and berries (as combined variable); cereals (rye, wheat, oats, and barley as combined variable); other cereals (maize, rice, millet, and buckwheat as combined variable), meat; fish; egg; cabbage; spinach; and lettuce	3 months	0 1-2 >2
		4 months	0 1-2 3-4
		6 months	0-4 5-6 7-8 >8
		12 months	0-7 8-9 10-11 >11
13	Yogurt, butter (only butter, not margarine), cow's milk, cheese, egg, meat, fish, nuts, vegetables, fruits, and cereals	24 months	8 9-10 >11 Continuous scores
14	Six food groups (cereals, vegetables, fruits, meats, fish, and eggs) at 6 months; 11 food groups (cereals, vegetables, fruits, meats, fish and seafood, eggs, beans, peanut, other nuts, milk and milk products, and sweets) at 12 months	6 months	0 1-2 3-6 Continuous scores
		12 months	1-5 6-7 8-11 Continuous scores
15	(1) Vegetables (avocado, cauliflower, beans, broccoli, peas, cucumbers, carrots, potatoes, white cabbage, turnip cabbage, lenses, celery, asparagus, spinach, tomatoes, onion, vegetable juices); (2) fruit (apples, pineapples, apricots, bananas, pears, strawberries, peaches, citrus fruit, fruit juices); (3) cereal (bread/pretzels/rolls, cookies/cakes/rusk, rolled oats, muesli, millet, cornmeal/corn starch, wheat semolina/starch, noodles, rice/rice starch, spelt); (4) meat (poultry, lamb, veal/beef, pork, sausages); (5) egg; (6) dairy products (cow milk/cream, yogurt/quark/cheese); (7) fish; (8) other (nuts, soy products, cocoa/chocolate)	12 months by food items	0-26 27-30 31-34 35-48 Continuous scores
		12 months by food groups	0-5 6 7 8 Continuous scores
16	Vegetables, cereal, fruit, meat, dairy products, egg, fish, and other (eg, soybean, nuts, cacao, chocolate)	4 months	1-2 3-8

(Continued)

TABLE IV. *(Continued)*

Study	Introduced complementary food	Exposure grouping measure	
		Exposure time	Diversity groups
17	Cow's milk, roots (potatoes, carrot, turnip); fruits and berries; wheat, rye, oats, and barley; meat; fish; egg; and other cereals (maize, rice, millet, buckwheat)	3 months	0 1-2 ≥3
		4 months	0 1-2 3-4 >4
		6 months	0-4 5-6 7-8 >8
18	Vegetables, cereal, fruit, meat, dairy products, egg, fish, and other (soybean, nuts, cocoa, chocolate)	4 months	0 1-2 3-8
		6 months	0 1-2 3-4 5-8
19	Cow's milk, eggs, vegetables, fruit, meat and dairy products	4 months	0 1-3 >4
20	Vegetables or fruits, cereals, bread, meat, cake, and yogurt	12 months	0-3 4-5 6 Continuous scores
21	Vegetables, legumes, or roots (potatoes, carrots, tomatoes, and beans), fruit (apples/pears, peaches/ apricots/plums, citrus fruits, and red fruits), cereals (maize/ tapioca, rice, pasta, and gluten-free pasta), meat (poultry, pork, and beef), dairy products (cheese and other dairies), fish, eggs, and nuts/cacao/ chocolate	4 months	0 1-2 3-22
		5 months	0 1-7 8-22
22	Dairy products, egg, cereals, legumes, vegetables, fruits, nuts, meat products, fish, and other foods	24 weeks	0 1-2 >2
23	Grains/roots/tubers, legumes/nuts, dairy, flesh foods, eggs, vitamin A rich fruit and vegetables, other fruits and vegetables		Continuous scores
24	Grains, vegetables, fruits, meat, fish, eggs, dairy, wheat, peanuts, and legumes/nuts		Continuous scores
25	Fruits (citrus fruit, noncitrus fruit, strawberries, tomato), vegetables, potato, pulses, nonwheat cereals (rice, oats), meat (chicken/turkey, lamb, beef, pork), and food allergens (cow's milk products, egg, wheat, peanut, tree nuts, fish, soy, sesame)		Continuous scores

In recent years, the prevention of allergic disease has gradually developed from passive avoidance of allergens to active induction of oral tolerance. Two systematic reviews published in 2019 concluded that introducing solid foods at approximately 4 to 6 months can reduce the risk of allergies to certain foods.[7,8] Therefore, we questioned the role of food diversity in preventing allergic disease. Food diversity reflects the number and frequency of individuals consuming a particular food or food group over a period of time. Since 1981 and the study by Fergusson et al,[26] attention has been given to the relationship between food diversity during infancy and the risk of later allergic disease, although the conclusions are not uniform. In 2020, the EAACI recommended increasing food diversity in infancy to prevent later allergic disease,[9] but no studies have integrated the available evidence to influence the implementation of diversified feeding strategies for infants and young children.

Notably, in the included studies, although 15 articles described the definition of food diversity, the methods used to assess diet diversity were varied, including diet diversity,[11-24] food diversity,[15,23,24] food allergen diversity,[15,24] and fruit and vegetable

diversity.[15] In addition, we found that the standards for classifying high or low food diversity were not wholly consistent among the studies. In the statistical analysis, some studies set the food diversity cutoff point by themselves, while other studies quantified and scored food types and analyzed them as continuous variables (Table IV). All the above factors may have a meaningful impact on the study's conclusions. In addition, the included studies divided the diversity according to the number of foods or the number of food groups. The amount or frequency of various foods ingested in infancy has not been analyzed, and it is not easy to distinguish between the effects of consuming large amounts of specific foods and contacting only specific foods on the occurrence of allergic disease. Nwaru et al[12] suggested that supplements and other micronutrients should be included in the calculation of food diversity to thoroughly reflect the association between food diversity and allergic disease. Finally, as a result of differences in geographic regions and cultural backgrounds, the dietary guidelines followed by the study populations and the main food types consumed by infants are not precisely the same, which may also be one of the reasons why the research conclusions are not entirely consistent. For example, in the studies of Zhong et al[14] and Stampfli et al,[13] among others, almost all infants at 12 months of age were introduced to vegetables, fruits, and meat, but a small number of people ate only peanuts and other nuts. Stampfli et al[13] found that the group with high food diversity consumed more dairy products, eggs, and other foods than the group with a low level of food diversity. After adjustment, it was found that eating dairy products may have a protective effect on allergic disease. Venter et al[23] suggested that the diversity of fruits and vegetables at 9 months old has a preventive effect on food allergy within 10 years, suggesting that food intake may play an essential role in preventing allergic disease. Subsequent studies may need to adopt a unified assessment method for food diversity and observe the relationship between food type, frequency, quantity, diversity, and atopic disease.

Interestingly, some studies have shown that food diversity in infants and young children has varied effects on different allergic disease risks at different ages. The studies of Venter et al[23] and Nwaru et al[12] did not find a link between food diversity and atopic disease at 3 and 4 months old. Zhong et al[14] found that food diversity at 6 months old had a preventive effect on skin-related atopic disease while there was no protective effect on food allergy, but food diversity at 12 months old had a preventive effect on food allergy and AD. Stampfli et al[13] reported that even if food diversity is high in the first year of life, insufficient food diversity in the second year remains a risk factor for developing allergic disease later in life. It can be seen that only a variety of foods in a specific period may have a protective effect on atopic disease, and this protective effect may be time sensitive and requires the continuous intake of diverse foods. This may be similar to the results of the LEAP and LEAP-On study, which suggest that early intake of peanuts can prevent peanut allergy, but consumption must be at least 6 g per week to be effective.[27]

Of the included studies, 2, 3, and 2 articles reported, respectively, that food diversity was not associated with eczema, allergic rhinitis, and inhalation allergen sensitization. After a comprehensive analysis of the literature, we found that the majority of studies (n = 11) included children aged 4 to 10 years at the end of the study. An extended follow-up time permits a longer time window from diversified dietary exposure to the occurrence of allergic outcomes, and some children may have developed immune tolerance to certain atopic disease, such as eczema. Yet in studies with a follow-up age of <4 years, the association of food diversity with asthma and allergic rhinitis was not investigated or found, which may be related to the difficulty in diagnosing asthma and allergic rhinitis in young children.[28] Insufficient follow-up time may mask the effect of food diversity on respiratory allergic disease. Therefore, follow-up studies should assess allergy outcomes multiple times at different time points during long-term follow-up to better clarify the relationship between early food diversity and allergic disease at different times. In addition, of the included studies, 2 articles reported a significant positive association between food diversity and eczema.[16,18] In the 2 studies, the authors investigated the effect of food diversity on eczema in infants before 6 months of age. Because infants were mainly breast-fed within 6 months of age, it is speculated that this result may be related to the fact that these studies did not exclude the protective effect of breast-feeding on eczema risk.[29,30]

Limitations

Because of the small number of included studies and the lack of raw data for most studies, quantitative analysis of the literature was not possible. The lack of accepted definitions and grouping criteria for food diversity is a fundamental reason for the heterogeneity of results across studies. Finally, the population included in the study mainly reside in developed European countries, and whether the results can be applied to other populations needs further research to confirm.

Conclusions and implications

The results of existing high-quality cohort studies show that increasing the variety of complementary foods in infancy can effectively prevent food allergy (5/5), and moderate evidence shows that increasing food variety can reduce the risk of asthma (4/6), AD (3/5), and food sensitization (3/5). However, the conclusions about its impact on eczema, allergic rhinitis, and other diseases are still controversial. Later clinical studies need a unified food diversity assessment and analysis method to verify the link between food diversity in infancy and atopic disease.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Halken S. Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention. Pediatr Allergy Immunol 2004;15(suppl 16):4-32.
2. Frei R, Heye K, Roduit C. Environmental influences on childhood allergies and asthma—the farm effect. Pediatr Allergy Immunol 2022;33:e13807.
3. Singh A, Holvoet S, Mercenier A. Dietary polyphenols in the prevention and treatment of allergic diseases. Clin Exp Allergy 2011;41:1346-59.
4. Kucuksezer UC, Ozdemir C, Cevhertas L, Ogulur I, Akdis M, Akdis CA. Mechanisms of allergen-specific immunotherapy and allergen tolerance. Allergol Int 2020;69:549-60.
5. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR Jr, Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: summary of the National Institute of Allergy and Infectious Diseases–sponsored expert panel. Pediatr Dermatol 2017;34:5-12.
6. Netting MJ, Campbell DE, Koplin JJ, Beck KM, McWilliam V, Dharmage SC, et al. An Australian consensus on infant feeding guidelines to prevent food allergy:

outcomes from the Australian Infant Feeding Summit. J Allergy Clin Immunol Pract 2017;5:1617-24. Erratum in: J Allergy Clin Immunol Pract 2018;6:323.
7. Obbagy JE, English LK, Wong YP, Butte NF, Dewey KG, Fleischer DM, et al. Complementary feeding and food allergy, atopic dermatitis/eczema, asthma, and allergic rhinitis: a systematic review. Am J Clin Nutr 2019;109(suppl 7): 890S-934S.
8. Burgess JA, Dharmage SC, Allen K, Koplin J, Garcia-Larsen V, Boyle R, et al. Age at introduction to complementary solid food and food allergy and sensitization: a systematic review and meta-analysis. Clin Exp Allergy 2019;49:754-69.
9. Venter C, Greenhawt M, Meyer RW, Agostoni C, Reese I, du Toit G, et al. EAACI position paper on diet diversity in pregnancy, infancy and childhood: novel concepts and implications for studies in allergy and asthma. Allergy 2020;75:497-523.
10. Wells GASB, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed April 25, 2016.
11. Roduit C, Frei R, Depner M, Schaub B, Loss G, Genuneit J, et al. Increased food diversity in the first year of life is inversely associated with allergic diseases. J Allergy Clin Immunol 2014;133:1056-64.
12. Nwaru BI, Takkinen HM, Kaila M, Erkkola M, Ahonen S, Pekkanen J, et al. Food diversity in infancy and the risk of childhood asthma and allergies. J Allergy Clin Immunol 2014;133:1084-91.
13. Stampfli M, Frei R, Divaret-Chauveau A, Schmausser-Hechfellner E, Karvonen AM, Pekkanen J, et al. Inverse associations between food diversity in the second year of life and allergic diseases. Ann Allergy Asthma Immunol 2022;128:39-45.
14. Zhong C, Guo J, Tan T, Wang H, Lin L, Gao D, et al. Increased food diversity in the first year of life is inversely associated with allergic outcomes in the second year. Pediatr Allergy Immunol 2022;33:e13707.
15. Markevych I, Standl M, Lehmann I, von Berg A, Heinrich J. Food diversity during the first year of life and allergic diseases until 15 years. J Allergy Clin Immunol 2017;140:1751, 4.e4.
16. Zutavern A, Brockow I, Schaaf B, von Berg A, Diez U, Borte M, et al. Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA. Pediatrics 2008;121:e44-52.
17. Nwaru BI, Takkinen HM, Niemelä O, Kaila M, Erkkola M, Ahonen S, et al. 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.
18. Filipiak B, Zutavern A, Koletzko S, von Berg A, Brockow I, Grübl A, et al. Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study. J Pediatr 2007;151:352-8.
19. Fergusson DM, Horwood LJ. Early solid food diet and eczema in childhood: a 10-year longitudinal study. Pediatr Allergy Immunol 1994;5(6 suppl):44-7.
20. Roduit C, Frei R, Loss G, Büchele G, Weber J, Depner M, et al. Development of atopic dermatitis according to age of onset and association with early-life exposures. J Allergy Clin Immunol 2012;130:130-6.e5.
21. Turati F, Bertuccio P, Galeone C, Pelucchi C, Naldi L, Bach JF, et al. Early weaning is beneficial to prevent atopic dermatitis occurrence in young children. Allergy 2016;71:878-88.
22. Schoetzau A, Filipiak-Pittroff B, Franke K, Koletzko S, Von Berg A, Gruebl A, et al. Effect of exclusive breast-feeding and early solid food avoidance on the incidence of atopic dermatitis in high-risk infants at 1 year of age. Pediatr Allergy Immunol 2002;13:234-42.
23. Venter C, Maslin K, Holloway JW, Silveira LJ, Fleischer DM, Dean T, et al. Different measures of diet diversity during infancy and the association with childhood food allergy in a UK birth cohort study. J Allergy Clin Immunol Pract 2020;8:2017-26.
24. Lee BR, Jung HI, Kim SK, Kwon M, Kim H, Jung M, et al. Dietary diversity during early infancy increases microbial diversity and prevents egg allergy in high-risk infants. Immune Netw 2022;22:e17.
25. Maslin K, Pickett K, Ngo S, Anderson W, Dean T, Venter C. Dietary diversity during infancy and the association with childhood food allergen sensitization. Pediatr Allergy Immunol 2022;33:e13650.
26. Fergusson DM, Horwood LJ, Beautrais AL, Shannon FT, Taylor B. Eczema and infant diet. Clin Allergy 1981;11:325-31.
27. du Toit G, Sayre PH, Roberts G, Lawson K, Sever ML, Bahnson HT, et al. Allergen specificity of early peanut consumption and effect on development of allergic disease in the Learning Early About Peanut Allergy study cohort. J Allergy Clin Immunol 2018;141:1343-53.
28. Lodge CJ, Tan DJ, Lau MX, Dai X, Tham R, Lowe AJ, et al. Breastfeeding and asthma and allergies: a systematic review and meta-analysis. Acta Paediatr 2015; 104(467):38-53.
29. Bigman G. The relationship of breastfeeding and infant eczema: the role of reverse causation. Breastfeed Med 2020;15:114-6.
30. Elbert NJ, van Meel ER, den Dekker HT, de Jong NW, Nijsten TEC, Jaddoe VWV, et al. Duration and exclusiveness of breastfeeding and risk of childhood atopic diseases. Allergy 2017;72:1936-43.