

## Clinical Commentary Review

# Preventing Food Allergy by Early Food Introduction: East Meets West With the Lack Dual-Allergen Exposure Theory

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Food allergy (FA) is a growing global health concern with inconclusive, although recent Japanese data suggest inevitable prevalence varying by region, influenced by genetic, environmental, and cultural factors. Eczema represents the strongest early-life risk factor, which supporting the Lack dual-allergen exposure hypothesis in which disrupted skin barriers facilitate sensitization, whereas timely oral exposure promotes tolerance. Over recent decades, prevention strategies have shifted from allergen avoidance to early introduction, particularly after the Learning Early About Peanut Allergy study. Although early egg introduction has been associated with a reduced risk of egg allergy in some studies, others have reported no significant effect. In contrast, early peanut introduction has strong preventive effects in Western countries with high peanut allergy prevalence, but it appears less impactful in Japan, where peanut consumption and prevalence are low. The role of early cow's milk introduction remains

benefit from small daily intake. Effective eczema management, including proactive anti-inflammatory therapy, may be crucial, because moisturizers alone are insufficient for FA prevention. Sustained and regular allergen intake after early introduction is likely to support long-term tolerance further. Prevention strategies must also account for cultural feeding practices, family dietary habits, and regional epidemiology, because these factors shape feasibility and public health relevance. Supporting a smooth transition to family foods, such as encouraging infants to share family meals without unnecessary restrictions, may help sustain tolerance and promote healthy eating patterns. Collaboration between Eastern and Western medical communities will be essential to harmonize evidence with cultural practices and develop effective, personalized FA prevention strategies worldwide. © 2025 The Authors.

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**Abbreviations used**

ASCI- Australasian Society of Clinical Immunology and Allergy  
 BSACI- British Society for Allergy & Clinical Immunology  
 EAACI- European Academy of Allergy & Clinical Immunology  
 ED- Eliciting dose  
 FA- Food allergy  
 SPADE- Strategy for Prevention of Milk Allergy by Daily Ingestion  
 of Infant Formula in Early Infancy

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**Key words:** Food allergy; Early allergen introduction; Atopic dermatitis; Dual-allergen exposure hypothesis; Eczema management; Peanut; Egg; Cultural differences; Allergy prevention; East–West comparison

**INTRODUCTION**

The epidemiology of food allergy (FA) varies globally, influenced by genetic, environmental, and dietary factors.<sup>1–5</sup> A meta-analysis estimated the global FA prevalence at 4.3% (95% CI, 3.8–4.7), with rates of 4.2% in Asia, 3.2% in the Americas, 4.8% in Europe, 1.6% in Africa, and 7.5% in Oceania.<sup>3</sup> Milk and egg were historically the most common, particularly in infants and young children.<sup>3</sup> However, peanut and nut allergies are increasingly prevalent, particularly in urbanized regions.<sup>4,6</sup>

Key risk factors in early childhood include male sex and a family history of allergic disease. Eczema is recognized as the strongest risk factor,<sup>3,7</sup> underscoring the importance of skin barrier dysfunction and early immune dysregulation. The Lack dual-allergen exposure theory<sup>8</sup> was originally proposed as a hypothesis but is now widely regarded as an established theory supported by multiple random controlled trials,<sup>9–15</sup> confirming its validity. It proposes that sensitization primarily occurs through a disrupted, inflamed skin barrier, particularly in infants with eczema, whereas early oral exposure promotes tolerance. Supporting this, various food allergens have been detected in the environment,<sup>16–18</sup> and environmental peanut exposure such as peanut proteins in household dust has been linked to increased sensitization in children with eczema.<sup>19</sup>

Lifestyle and environmental changes may further explain rising FA prevalence.<sup>20</sup> The epithelial barrier hypothesis<sup>21</sup> and hygiene hypothesis<sup>22</sup> highlight how pollution, Westernized diets, smaller family size, and reduced microbial exposure can impair immune tolerance. Some observational studies suggested that early antacid use might increase allergy risk. However, a recent systematic review did not find a significant association for FA, leaving the evidence inconclusive.<sup>23</sup>

International guidelines (eg, the Joint CSACI, the American Academy of Allergy, Asthma & Immunology and ACAAI,<sup>24</sup> the British Society for Allergy & Clinical Immunology (BSACI),<sup>25</sup> the Australasian Society of Clinical Immunology and Allergy (ASCI),<sup>26</sup> the European Academy of Allergy & Clinical Immunology (EAACI),<sup>27</sup> the Asia Pacific Association of Pediatric Allergy, Respiriology & Immunology,<sup>28</sup> and the Japanese

Society of Pediatric Allergy and Clinical Immunology<sup>29</sup> emphasize early allergen introduction as a key strategy for preventing FA; some guidelines also recommend eczema care.<sup>29</sup> A 2023 systematic review<sup>30</sup> noted inconsistencies across guidelines and emphasized the need for harmonization. Although these principles are globally relevant, cultural and dietary differences between the East and West require regionally adapted approaches.

**HISTORICAL PERSPECTIVES ON FA PREVENTION**

Approaches to FA prevention have evolved over recent decades, shaped by cultural practices and emerging evidence. In Western countries, guidelines in the 1990s and early 2000s recommended allergen avoidance, especially for infants at high risk.<sup>31</sup> However, around 2008, recommendations<sup>32</sup> began shifting away from delayed introduction, and after the 2015 Learning Early About Peanut Allergy study,<sup>9</sup> guidelines more strongly endorsed early introduction of allergenic foods.

A pivotal observational study published in 2008, led by du Toit and Lack,<sup>33</sup> compared peanut allergy prevalence between Jewish children in Israel and the United Kingdom. The study found a markedly lower rate of peanut allergy in Israel, where early peanut consumption was common. This key finding laid the groundwork for the Learning Early About Peanut Allergy randomized trial (RCT), which confirmed that early introduction of peanut can prevent peanut allergy in infants at high risk.

As a result, organizations such as the BSACI,<sup>25</sup> ASCIA,<sup>26</sup> CSACI and ACAAI,<sup>24</sup> and EAACI<sup>27</sup> now recommend introducing allergenic foods in infancy. Whereas the EAACI highlights introduction at around 4 to 6 months, the American Academy of Allergy, Asthma & Immunology, ASCIA, and BSACI recommend introduction from around 6 months, with the BSACI noting that infants at greater risk may benefit from introduction from 4 months. Similarly, the US Dietary Guidelines state that “If an infant has severe eczema, egg allergy, or both (conditions that increase the risk of peanut allergy), age-appropriate, peanut-containing foods should be introduced as early as age 4 to 6 months.”<sup>34</sup>

In contrast, complementary feeding in Eastern countries often begins with rice porridge and vegetables, whereas peanuts and nuts are not commonly used as complementary foods during infancy. However, as dietary habits in many Eastern countries gradually westernize, there is a growing trend toward incorporating Western evidence into prevention strategies. Guidelines from organizations such as the Japanese Society of Pediatric Allergy and Clinical Immunology<sup>29</sup> increasingly integrate global evidence while adapting to cultural and dietary contexts.

For a better understanding of these differences, Table 1<sup>35–38</sup> compares infant complementary feeding practices between the East and West. For example, early peanut introduction<sup>39</sup> and the use of commercial baby foods<sup>40</sup> are common in Australia, whereas in Japan, early introduction of certain nuts is promoted in specialized allergy clinics.<sup>41</sup> These data illustrate diverse feeding practices and the need for culturally sensitive allergy prevention strategies, although evidence remains heterogeneous.<sup>30</sup>

**KEY EVIDENCE SUPPORTING EARLY INTRODUCTION**

We performed a meta-analysis of RCTs<sup>9–14,42–50</sup> evaluating the early introduction of major allergenic foods (egg, milk, and peanut) and their effects on FA incidence (Figures 1–4). This

**TABLE 1.** Comparison of infant complementary feeding practices: East vs West<sup>29-32</sup>

Aspect	East (Asia)	West (Europe/North America, including Australia)
Typical ingredients	Rice, vegetables, tofu, fish, fermented foods (eg, miso, natto)	Potatoes, meat, dairy products, fruits, vegetables, grains
Cooking methods	Boiling, steaming, minimal seasoning	Blending, pureeing, microwaving, often using commercial baby food
Flavor profile	Mild, natural flavors, often based on family meals	Varied flavors, sometimes sweetened or seasoned
Weaning style	Spoon-feeding, gradual texture progression (puree → mashed → solid)	Baby-led weaning increasingly popular: finger foods from age 6 mo, skipping pureed foods altogether.
Cultural influence	Strong reliance on family traditions and elders' advice	Influenced by pediatric guidelines and modern parenting trends
Introduction age	Around 6 mo (World Health Organization guideline), sometimes slightly earlier	Around 6 mo (World Health Organization guideline) complementary foods are recommended; however, most introduce complementary foods before age 6 mo.
Use of commercial food	Less common, homemade meals preferred	More common, wide variety of commercial baby food available
Nutritional focus	Balanced with rice and vegetables, emphasis on digestion	Emphasis on iron-rich foods (for the predominantly breastfed infant) and variety
Peanuts	Peanut are not commonly used as complementary foods. Although early introduction is being studied, national guidelines often do not explicitly recommend it. Whole peanuts should be given to children aged <6 y owing to choking hazards, as recommended by consumer safety authorities in Japan.	Early introduction (around 4-6 mo) of peanut is increasingly recommended based on the LEAP study, <sup>26</sup> especially for allergy prevention Ground peanut and other infant-safe forms of peanut are advised, because whole peanuts are a choking hazard to children aged <4 y in the American Academy of Pediatrics guidelines.
Tree nuts	Tree nuts are not commonly used as complementary foods. Although early introduction is being studied, national guidelines often do not explicitly recommend it. Whole tree nuts should not be given to children aged <6 y owing to choking hazards, as recommended by consumer safety authorities in Japan.	Introduce potentially allergenic foods such as infant-safe forms of tree nuts together with other complementary foods around age 6 mo in the United States. <sup>34</sup>

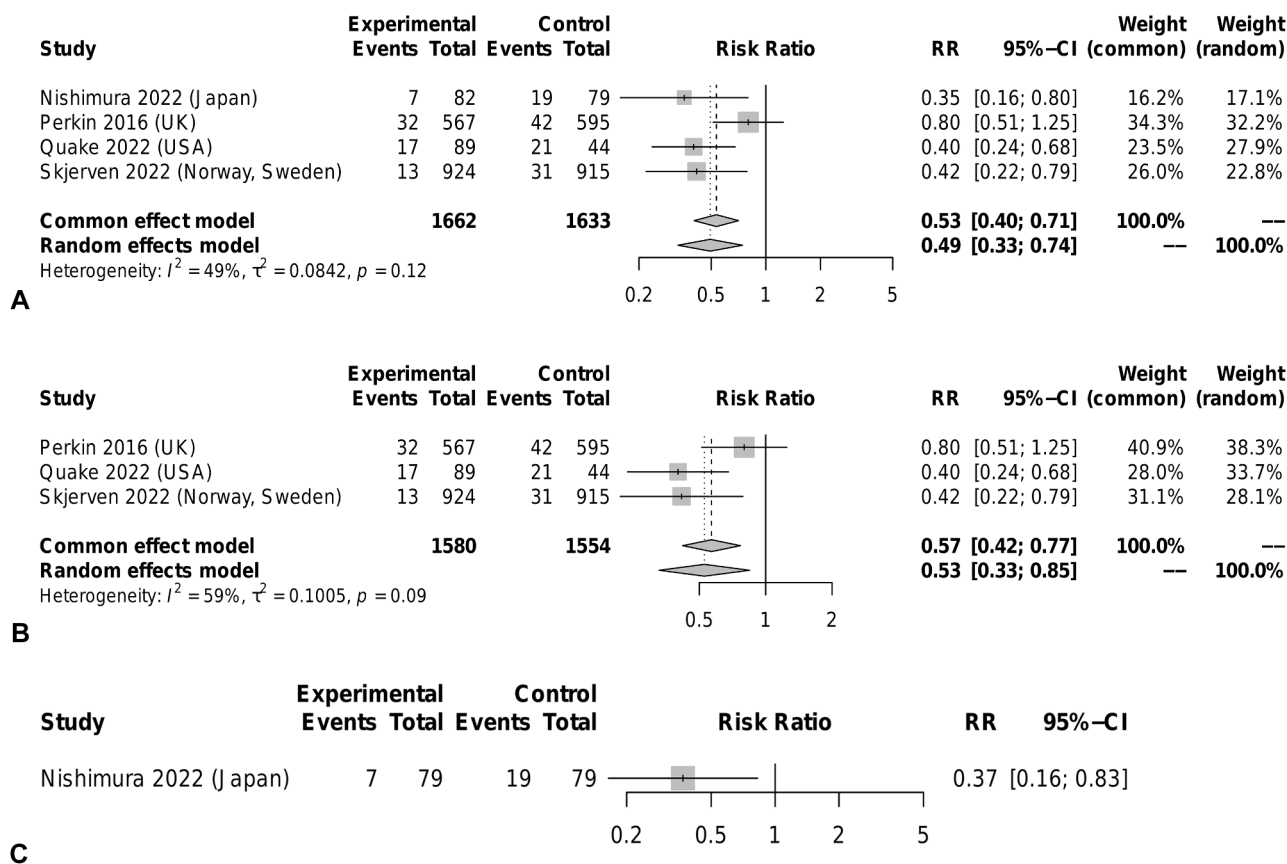
analysis builds on and updates the previously published systematic reviews and meta-analyses by Scarpone et al,<sup>51</sup> incorporating recent evidence including an additional RCT by the Strategy for Prevention of Milk Allergy by Daily Ingestion of Infant Formula in Early Infancy (SPADE) study<sup>13</sup> on cow's milk allergy prevention. All included studies were stratified by geographic region (Western vs Eastern countries). Scarpone et al did not conduct subgroup analyses by geographic regions, and the current review provides these results. We analyzed findings using fixed- and random-effects models and calculated risk ratios (RRs) and 95% CIs.

Our pooled analysis demonstrated that early allergen introduction significantly reduces FA risk (Figures 1, A-C). For any allergenic foods combined, early introduction yielded a pooled random-effects RR of 0.49 (95% CI, 0.33-0.74;  $I^2 = 49\%$ ;  $n = 4$  studies<sup>10-12,42</sup>) (Figure 1, A), consistent with findings reported in the systematic review by Scarpone et al.<sup>51</sup> Subgroup analyses confirmed consistent protective effects in the West (random-effects RR = 0.53 [0.33-0.85];  $I^2 = 59\%$ ;  $n = 3$  studies<sup>11,12,42</sup>) in Figure 1, B and the East (RR = 0.37 [0.16-0.83];  $n = 1$  study<sup>10</sup>) in Figure 1, C.

Regarding milk (Figure 2, A-C), the overall effect of early introduction was not statistically significant (pooled random-effects RR = 0.64 [0.26-1.56];  $I^2 = 55\%$ ;  $n = 7$

studies<sup>10,12,13,42-45</sup>) and exhibited substantial heterogeneity (Figure 2, A). Subgroup analysis revealed reduced heterogeneity in the four Western studies<sup>12,42-44</sup> (Figure 2, B), where no significant effect was detected, suggesting consistency in outcomes across these trials. In contrast, the Eastern subgroup of three studies<sup>10,13,45</sup> (Figure 2, C) showed high heterogeneity, indicating variability in study design, population characteristics, and implementation of early milk introduction protocols. However, the SPADE study (Japan)<sup>13</sup> suggested that daily ingestion of small amounts of milk formula combined with breastfeeding from age 1 month might reduce milk allergy risk in the general population (RR = 0.12 [0.03-0.52]). Intervention methods for milk varied across studies, and it was suggested that the preventive effect may differ depending on the amount and timing of intake. In addition, the study by Katz et al,<sup>52</sup> although observational in design, concluded that "early exposure to cow's milk protein as a supplement to breast-feeding might promote tolerance." This finding supports the hypothesis that early introduction of cow's milk protein could be beneficial, although further randomized controlled trials are needed to confirm this effect.

Egg introduction demonstrated the most consistent preventive effect across subgroups among allergens with a pooled random-effects RR of 0.59 (95% CI, 0.46-0.76;  $I^2 = 6\%$ ;  $n = 9$



**FIGURE 1.** (A) All food introductions in the West and the East. (B) All food introductions in the West. (C) All food introductions in the East. RR, relative risk.

studies<sup>10,12,14,42,46-50</sup>) (Figure 3, A), benefiting both Western (RR = 0.67 [0.51-0.88];  $I^2 = 0\%$ ; n = 7 studies<sup>12,42,46-50</sup>) (Figure 3, B) and Eastern (RR = 0.28 [0.14-0.54];  $I^2 = 0\%$ ; n = 2 studies<sup>10,14</sup>) populations (Figure 3, C). Introduction of well-cooked egg seems to be safer than raw, pasteurized egg for the prevention of egg allergy. Two Japanese RCTs (Natsume 2017<sup>14</sup> and Nishimura 2022<sup>10</sup>) provided strong support for early egg introduction with a small protein dose of heated-egg powder in infants with eczema whose eczema was well-controlled. In both studies, early egg introduction was conducted in the context of active eczema treatment, ensuring good control throughout the intervention period. This approach underscores the importance of managing skin inflammation before and during allergenic food introduction to reduce the risk of allergic sensitization.

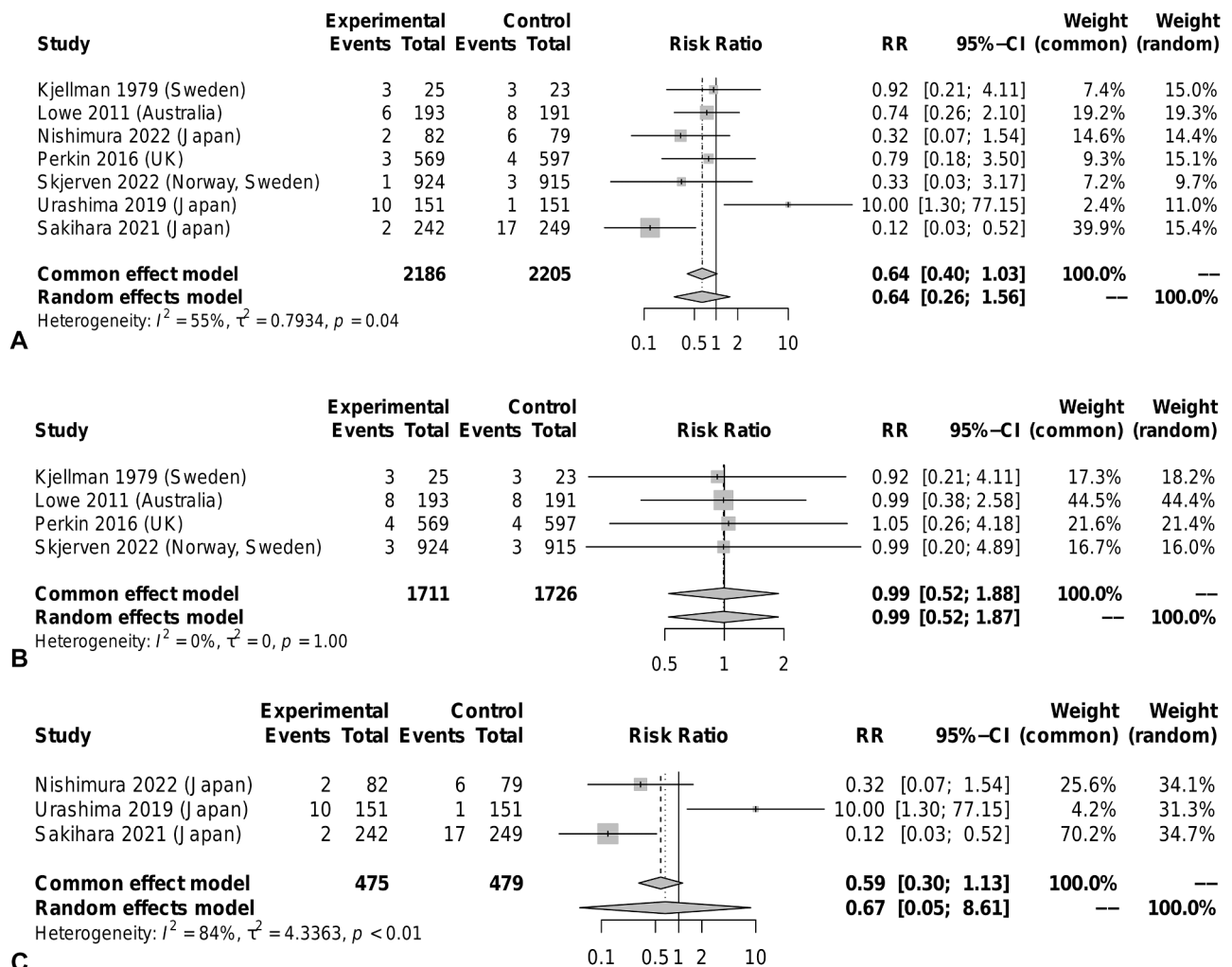
Peanut introduction was also significantly protective (pooled random-effects RR = 0.32 [0.18-0.56];  $I^2 = 21\%$ ; n = 4 studies<sup>9,10,12,42</sup>) (Figure 4, A), driven by a significant effect in Western data (pooled random-effects RR = 0.31 [0.17-0.56];  $I^2 = 45\%$ ; n = 3 studies<sup>9,12,42</sup>) (Figure 4, B). Conversely, the single study in the East (Japan)<sup>10</sup> did not observe a protective effect of early peanut introduction in infants with eczema (Figure 4, C), although the RR of 0.48 [0.04-5.21] is similar to that in the West, with wide CIs owing to the small sample size. Egg allergy is the most common, whereas the prevalence of peanut allergy is low in Japan,<sup>53</sup> which suggests that other cultural or dietary factors may influence these outcomes. On a

global scale, Japan's per capita peanut consumption is remarkably low, amounting to less than one tenth that in the United States.<sup>54</sup>

These findings indicate that although the early introduction of allergenic foods reduces FA risk, its magnitude differs between regions. Early egg introduction shows consistent preventive effects, whereas benefits of early peanut introduction are evident in Western countries with high prevalence, but are less pronounced in Japan. Kojima et al<sup>53</sup> reported only 0.2% peanut allergy at 4 years in a Japanese cohort, and early ingestion was not significantly protective. In Israel, where peanuts are commonly introduced early in infancy and widely consumed, the prevalence of peanut allergy is also low.<sup>33</sup> Thus, early introduction may be most beneficial for foods with both high consumption and high allergy prevalence. The effect of milk introduction remains inconclusive and may depend on timing, dose, and concurrent breastfeeding. Promising results from the SPADE study<sup>13</sup> in Japan warrant further research to assess whether similar protective effects occur in Western populations. Region-specific strategies considering epidemiology and dietary habits are needed, although definitive trials are constrained by ethics.

## THE ROLE OF ECZEMA MANAGEMENT IN FOOD ALLERGY PREVENTION

According to the dual-allergen exposure theory, proactive management of atopic dermatitis<sup>55</sup> is expected to reduce FA



**FIGURE 2.** (A) Milk introduction in the West and the East. (B) Milk introduction in the West. (C) Milk introduction in the East. *RR*, relative risk.

development. An observational study in Japan indicated that early intervention for eczema,<sup>56</sup> including proactive treatment targeting both clinical symptoms and subclinical inflammation, may decrease the risk of allergic sensitization.

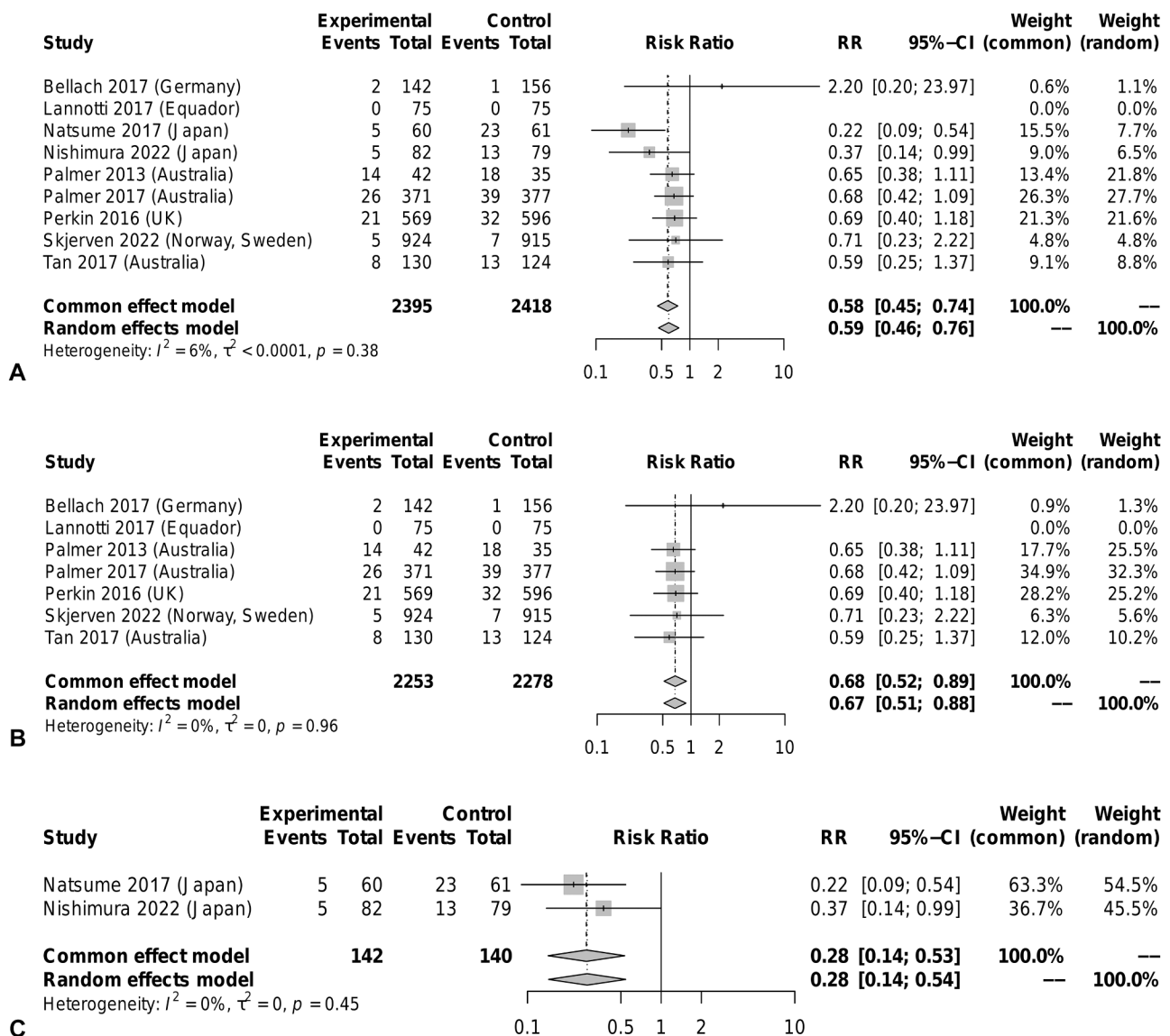
The Phase 3 Prevention of Allergy via Cutaneous Intervention study in Japan demonstrated that early targeted eczema treatment, such as proactive therapy with topical corticosteroids combined with skin barrier care, may reduce the risk of hen's egg allergy in children with early-onset eczema.<sup>15,57</sup> However, the authors cautioned that the enhanced treatment protocol should be modified before being considered for routine practice, owing to potential adverse effects such as significantly reduced growth in the aggressively treated group. A follow-up Prevention of Allergy via Cutaneous Intervention-ON (PACI-ON) cohort is currently investigating the long-term outcomes of this intervention.<sup>58</sup> Ongoing studies, including the Stopping Eczema and Allergy Study<sup>59</sup> (emollient therapy combined with topical corticosteroids) in the United States and United Kingdom and the DIFENSE study<sup>60</sup> (topical phosphodiesterase-4 inhibitors) in Japan, are expected to provide further robust evidence on

whether intensive skin management can effectively prevent FA development.

These findings emphasize the potential benefit of integrating early eczema management, particularly proactive therapy addressing subclinical inflammation, with timely allergenic food introduction as complementary strategies for FA prevention. Importantly, skin barrier reinforcement with moisturizers alone has not demonstrated sufficient preventive efficacy by systematic reviews.<sup>61,62</sup> This underscores the necessity of focusing eczema treatment on underlying inflammation rather than barrier repair alone.<sup>63</sup>

*Staphylococcus aureus* colonization is linked to higher rates of food allergen sensitization and may delay tolerance acquisition, emphasizing the role of microbial factors alongside eczema management in early allergen introduction.<sup>64</sup>

Infants with early-onset eczema,<sup>65,66</sup> uncontrolled eczema,<sup>67</sup> or persistent eczema<sup>68</sup> are at risk for FA. In the Prevention of Egg Allergy With Tiny Amount Intake study, infants who consumed eggs from an early age but had poorly controlled eczema still developed egg allergy. This suggests that early and



**FIGURE 3.** (A) Egg introduction in the West and the East. (B) Egg introduction in the West. (C) Egg introduction in the East. RR, relative risk.

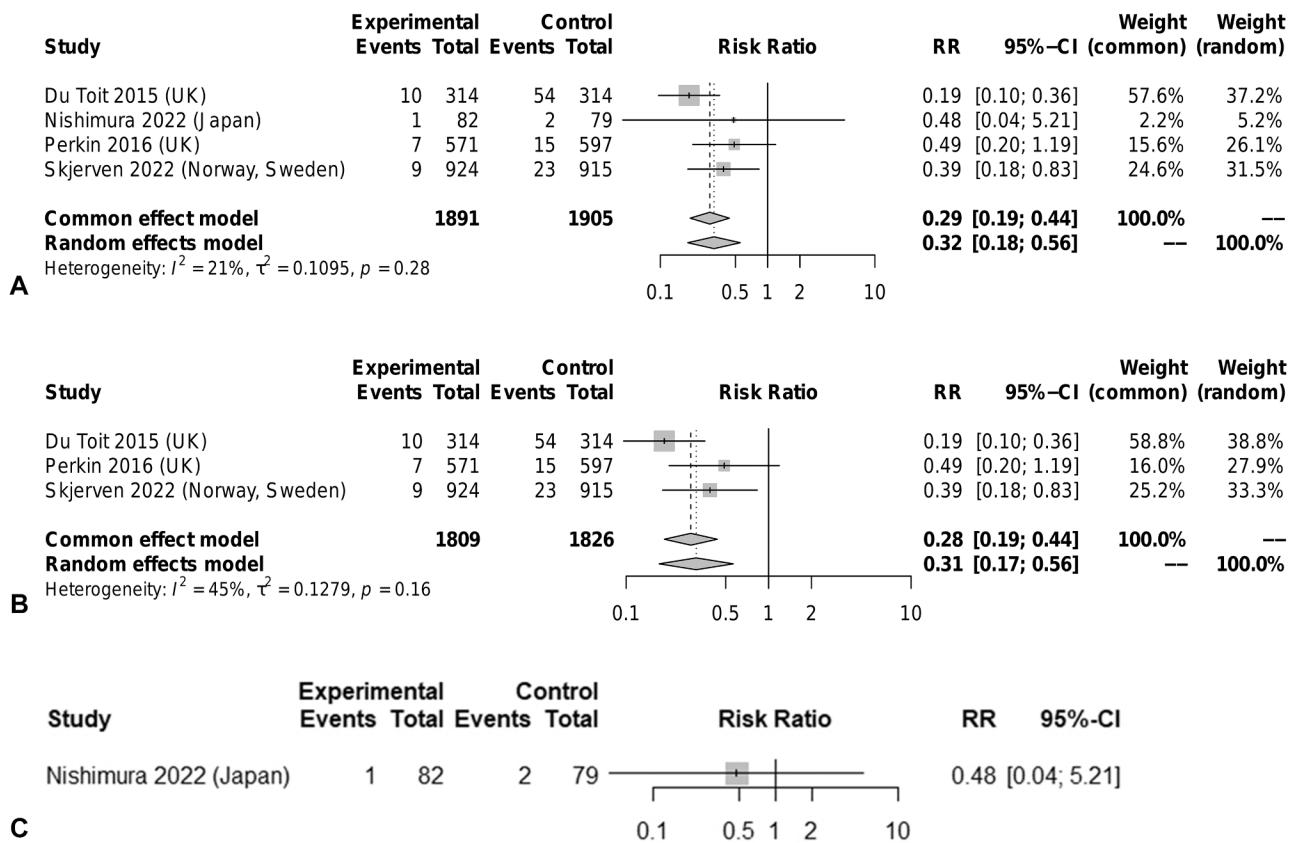
regular oral allergen intake alone may not be sufficient to prevent FA.

## IMPLEMENTATION IN CLINICAL PRACTICE: EAST VERSUS WEST

### Lack dual-allergen exposure theory and its clinical implications

The dual-allergen exposure theory underscores the critical importance of effective eczema management combined with the timely oral introduction of allergenic foods in preventing IgE-mediated FA. Infants with atopic dermatitis have increased susceptibility to percutaneous sensitization to allergens. Consequently, integrated management strategies that address both eczema and dietary interventions are likely essential to mitigate IgE-mediated FA risk. From a biological perspective, the fundamental mechanisms underlying allergy prevention, such as

oral tolerance induction, may be similar between Eastern and Western populations. However, the effectiveness of early introduction strategies may differ depending on local and family dietary habits and the prevalence of specific FAs. Current evidence regards cow's milk allergy prevention and eczema management primarily derived from Eastern populations, whereas evidence about peanut allergy prevention is primarily derived from Western populations. Thus, although the biological basis appears consistent, regional factors may influence the practical outcomes of prevention strategies. Early introduction of allergenic foods, even in small amounts, followed by regular and sustained ingestion of sufficient amounts of allergenic protein, can induce oral immune tolerance and thus prevent the development of IgE-mediated FA. Early introduction may be associated with an increased incidence of food protein-induced enterocolitis syndrome<sup>69</sup> in some cases (the condition remains rare), but FA prevention specifically targets immediate-type



**FIGURE 4.** (A) Peanut introduction in the West and the East. (B) Peanut introduction in the West. (C) Peanut introduction in the East. RR, relative risk.

reactions, and food protein-induced enterocolitis syndrome represents a distinct non IgE-mediated mechanism.

In infants with early-onset eczema, percutaneous sensitization often precedes oral exposure and is associated with elevated specific IgE levels.<sup>70</sup> Effective eczema treatment can reduce IgE levels,<sup>71,72</sup> which reinforces the need to manage skin inflammation before complementary feeding. Strategies aimed at reducing the degree of sensitization are important, because higher sensitization levels increase the risk of symptom elicitation and lower the threshold of allergen exposure to trigger a reaction.<sup>73,74</sup> In this population, pre-challenge risk assessment and supervised oral food challenge may ensure safe allergen introduction. Although routine prescreening with skin or specific IgE testing is not recommended, in-office introduction remains an option for families who prefer it. As guidelines increasingly move from recommending routine prescreening, this approach remains controversial and warrants further study.

Eczema, particularly early-onset and more severe forms, is a well-established risk factor for FA, but most infants worldwide do not have eczema. Importantly, cases of FA still develop in these infants at low risk. Therefore, consistent with recent Australian as well as US and Canadian consensus guidelines,<sup>24</sup> timely introduction of allergenic foods is recommended for all infants irrespective of eczema status, to promote immune tolerance.

### Regular and sustained allergenic food intake

Recent research highlights that regular intake of allergenic foods is crucial to prevent FA. Studies<sup>13,75</sup> show that regular

consumption of cow's milk after early introduction helps prevent cow's milk allergy, whereas discontinuation or intermittent exposure may increase allergy risk.<sup>76,77</sup> An observational study showed that egg consumption two or more times per week during late infancy is associated with a decreased risk of developing egg allergy in later childhood.<sup>78</sup> Similarly, Abrams et al<sup>79</sup> reported that early introduction followed by regular consumption of allergenic foods (eg, a few times a week) significantly reduces the risk of developing allergies.

### Eliciting dose and allergen-specific considerations

In infants aged 12 months or younger with FA, eliciting doses (EDs) predicted to provoke objective reactions in 5% of allergic individuals were estimated at 28.6 mg for egg white protein, 6.1 mg for milk protein, and 27.7 mg for wheat protein.<sup>80</sup> These ED values are higher than those observed in older children and tend to decrease with age. Table II provides approximate examples of typical food portions corresponding to the ED values for egg, milk, and wheat proteins in infants.

Notably, ED values vary across allergens, and nuts and peanuts show much lower EDs predicted to provoke objective reactions in 5% of allergic individuals (Table III).<sup>83</sup> Taken together, these findings suggest that initial allergenic protein doses for infant introduction should be small, especially for infants with eczema or elevated IgE levels who are at high risk. Subsequently, gradual dose escalation can occur based on tolerance.

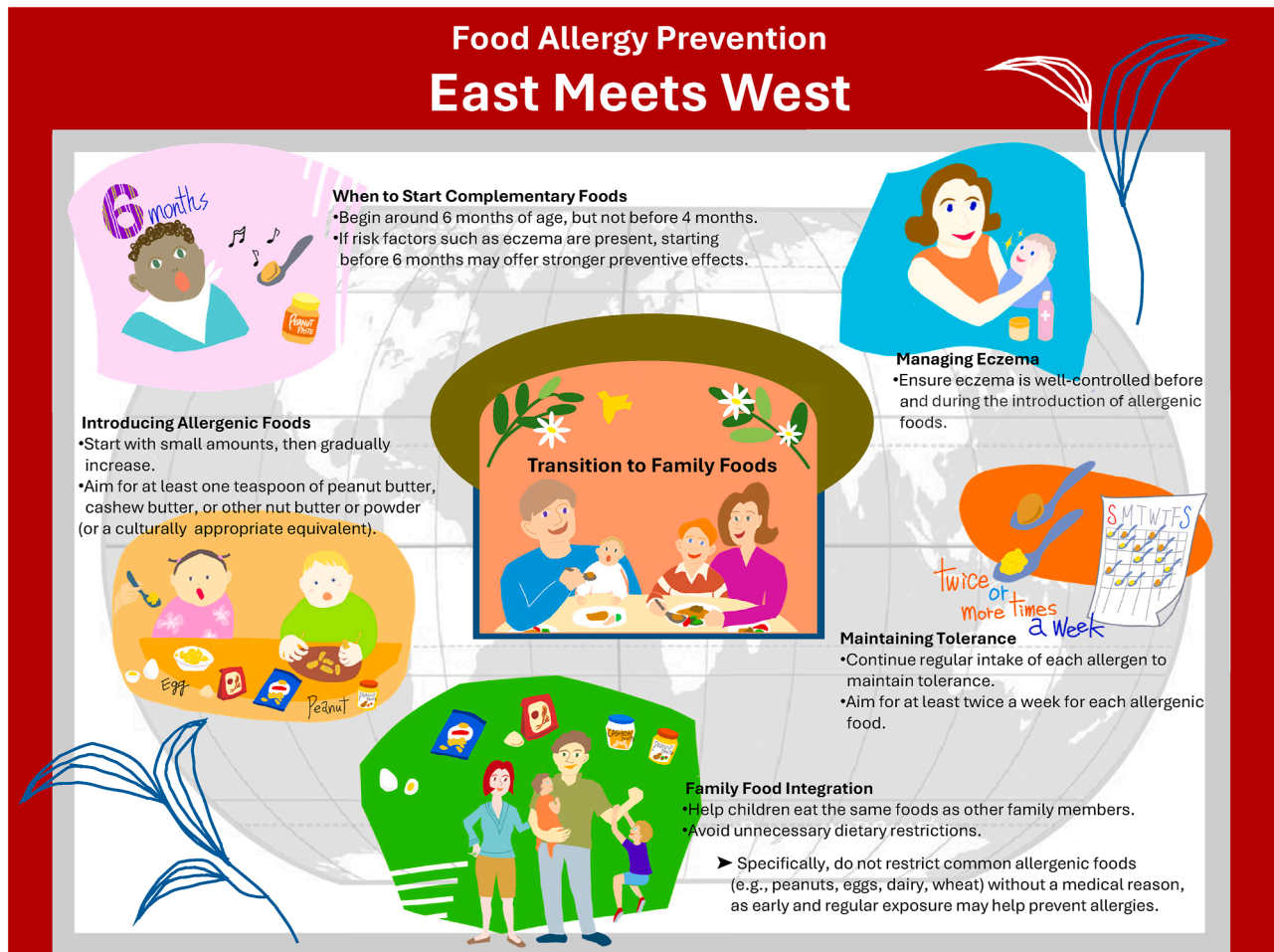


FIGURE 5. Summary of preventing food allergy by early food introduction: East meets West.

### Commercial allergen introduction products

In the United States and Japan, many commercial products are marketed for the early introduction of allergenic foods.<sup>84</sup> However, most lack proven preventive effects, may contain less protein than indicated, and have occasionally triggered allergic reactions, including bodily responses to the natural food after using such products. This highlights the need to verify the products' allergen-specific protein content.<sup>85</sup> Their use, especially in infants at high risk, should occur only under professional supervision.

### CULTURAL AND REGIONAL VARIATIONS: EAST VERSUS WEST

Food allergy prevention strategies must reflect cultural, environmental, and family dietary differences between Eastern and Western populations. Dietary customs, prevalent allergens, food preparation methods, and the timing and frequency of allergen introduction necessitate region-specific guidelines.

For example, infants born in Australia with parents born in East Asia had approximately threefold higher rates of peanut sensitization and allergy compared with those with Australian-born parents,<sup>86</sup> illustrating complex gene–environment interactions. In Australia, infants who developed FA despite

allergen introduction by 6 months were more likely to have Asian-born parents and early-onset moderate to severe eczema.<sup>87</sup> Furthermore, earlier introduction of peanut was associated with a reduced risk of peanut allergy in infants with Australian-born parents, but not in those with Asian-born parents.<sup>39</sup> In a nationally representative survey of the US population, the prevalence of FA was found to be higher among Asian, Hispanic, and non-Hispanic Black individuals compared with non-Hispanic White individuals.<sup>88</sup> Personalized management of allergic diseases requires integration of patients' genetic predisposition and relevant environmental exposures.

In Japan, most infants with eczema are sensitized to egg by 6 months. This makes egg allergy the most common FA and emphasizes the importance of early egg introduction. In contrast, peanut sensitization is rare by 1 year, which suggests that early peanut introduction may be less critical. Nevertheless, evidence from other countries indicates that early nut introduction could be beneficial if it is culturally acceptable.<sup>89</sup> However, data from Australia showing a low prevalence of cashew sensitization and allergy in those with early introduction highlight the potential benefits of early nut introduction if it is culturally acceptable.<sup>90</sup>

IgE sensitization alone does not confirm FA, yet strict avoidance diets are still often recommended by primary

**TABLE II.** Example food amounts of 30 mg of protein

Allergen	Example food amount of ~30 mg protein
Hen's egg	1/200th of a whole egg
Milk	1 mL liquid milk 0.8 g yogurt*
Wheat	0.3 g wheat flour 1 cup of small elbow macaroni† 0.56 g udon (cooked)‡

\*About 0.729-0.850 g based on 170 g yogurt containing 6 or 7 g protein (depending on the fat content).

†This is based on the classic size of elbow noodles in the United States.<sup>81</sup>

‡Cooked udon noodles are about 5.31% protein based on the US Department of Agriculture FoodData Central.<sup>82</sup>

**TABLE III.** Food-allergenic population eliciting dose<sup>83</sup>

Food item	Eliciting dose (amount of protein) predicted to provoke objective reactions in 5% of allergic individuals, mg (95% CI)	Food quantity
Cashew	1.6 (0.4-9.4)	0.008 g
Hen's egg	2.4 (1.3-5.3)	0.02 g
Fish	15.6 (4.6-102)	0.078 g
Hazel	4.7 (1.7-15.7)	0.035 g
Milk	3.1 (1.6-6.6)	0.09 mL
Peanut	3.9 (2.8-7.1)	0.116 g
Sesame	4.2 (0.6-57.7)	0.021 g
Shrimp	429 (94.0-1,854)	2.1 g
Walnut	1.2 (0.1-13.0)	0.008 g
Wheat	9.3 (3.9-24.9)	0.36 g

physicians and specialists, potentially delaying tolerance. Proper evaluation, including oral food challenges, can prevent unnecessary avoidance and support safe early introduction. The number of families who do not reintroduce foods after an oral food challenge remains high, underscoring the need for high-quality data to support families in implementing safe reintroduction.<sup>91</sup> Education for health care professionals, caregivers, and the public is also essential to promote evidence-based practices in eczema control, allergen introduction, and avoidance of unnecessary food restrictions.<sup>92-94</sup>

## CONCLUSION

Ultimately, region-specific strategies are needed that build on the dual-allergen exposure theory, now evolved from hypothesis through accumulating trial evidence, integrating early allergen introduction with proactive eczema management, tailored dietary guidance, and cultural sensitivity. Supporting a smooth transition to family foods, encouraging children to eat the same meals as their family while avoiding unnecessary restrictions, can help sustain tolerance and foster healthy eating habits. Collaboration between Eastern and Western medical communities can support personalized prevention, especially for culturally diverse populations.

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## REFERENCES

- Leung AS-Y, Pacharn P, Tangvalelerd S, Sato S, Pitt E, Wong G, et al. Food allergy in a changing dietary landscape: a focus on the Asia Pacific region. *Pediatr Allergy Immunol* 2024;35:e14211.
- Peters RL, Soriano VX, Allen KJ, Tang MLK, Perrett KP, Lowe AJ, et al. The prevalence of IgE-mediated food allergy and other allergic diseases in the first 10 years: the population-based, longitudinal HealthNuts study. *J Allergy Clin Immunol Pract* 2024;12:1819-30.e3.
- Feng H, Xiong X, Chen Z, Xu Q, Zhang Z, Luo N, et al. Prevalence and influencing factors of food allergy in global context: a meta-analysis. *Int Arch Allergy Immunol* 2023;184:320-52.
- Spolidoro GCI, Ali MM, Amara YT, Nyassi S, Lisik D, Ioannidou A, et al. Prevalence estimates of eight big food allergies in Europe: updated systematic review and meta-analysis. *Allergy* 2023;78:2361-417.
- Miyaji Y, Yang L, Harama D, Saito-Abe M, Sato M, Sakamoto K, et al. Trajectories of IgE, IgA and IgG levels in preschool-aged children: insights from the subcohort study of the Japan Environment and Children's Study. *Clin Exp Allergy* 2025;55:808-19.
- Lange L, Klimek L, Beyer K, Blumchen K, Novak N, Hamelmann E, et al. White paper on peanut allergy - part 1: epidemiology, burden of disease, health economic aspects. *Allergo J Int* 2021;30:261-9.
- Peters RL, Mavoa S, Koplin JJ. An overview of environmental risk factors for food allergy. *Int J Environ Res Public Health* 2022;19:722.
- Lack G. Epidemiologic risks for food allergy. *J Allergy Clin Immunol* 2008; 121:1331-6.
- Du Toit G, Roberts G, Sayre PH, Bahnsen HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med* 2015;372:803-13.
- Nishimura T, Fukazawa M, Fukuoka K, Okasora T, Yamada S, Kyo S, et al. Early introduction of very small amounts of multiple foods to infants: a randomized trial. *Allergol Int* 2022;71:345-53.
- Quake AZ, Liu TA, D'Souza R, Jackson KG, Woch M, Tetteh A, et al. Early introduction of multi-allergen mixture for prevention of food allergy: pilot study. *Nutrients* 2022;14:737.
- Skjerven HO, Lie A, Vettukattil R, Rehbinder EM, LeBlanc M, Asarnoj A, et al. Early food intervention and skin emollients to prevent food allergy in young children (PreventADALL): a factorial, multicentre, cluster-randomised trial. *Lancet* 2022;399:2398-411.
- Sakihara T, Otsuji K, Arakaki Y, Hamada K, Sugiura S, Ito K. Randomized trial of early infant formula introduction to prevent cow's milk allergy. *J Allergy Clin Immunol* 2021;147:224-32.e8.
- Natsume O, Kabashima S, Nakazato J, Yamamoto-Hanada K, Narita M, Kondo M, et al. Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial. *Lancet* 2017;389:276-86.
- Yamamoto-Hanada K, Kobayashi T, Mikami M, Williams HC, Saito H, Saito-Abe M, et al. Enhanced early skin treatment for atopic dermatitis in infants reduces food allergy. *J Allergy Clin Immunol* 2023;152:126-35.
- Trendelenburg V, Tschirner S, Niggemann B, Beyer K. Hen's egg allergen in house and bed dust is significantly increased after hen's egg consumption-a pilot study. *Allergy* 2018;73:261-4.
- Kitazawa H, Yamamoto-Hanada K, Saito-Abe M, Ayabe T, Mezawa H, Ishitsuka K, et al. Egg antigen was more abundant than mite antigen in children's bedding: findings of the pilot study of the Japan Environment and Children's Study (JECS). *Allergol Int* 2019;68:391-3.
- Yasudo H, Yamamoto-Hanada K, Mikuriya M, Ogino F, Fukuie T, Ohya Y. Association of walnut proteins in household dust with household walnut consumption and Jug r 1 sensitization. *Allergol Int* 2023;72:607-9.
- Brough HA, Liu AH, Sicherer S, Makinson K, Douiri A, Brown SJ, et al. Atopic dermatitis decreases the effect of exposure to peanut antigen in dust on peanut sensitization and likely peanut allergy. *J Allergy Clin Immunol* 2015; 135:164-70.
- Rennie GH, Zhao J, Camus-Ela M, Shi J, Jiang L, Zhang L, et al. Influence of lifestyle and dietary habits on the prevalence of food allergies: a scoping review. *Foods* 2023;12:3290.
- Akdis CA. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions? *Nat Rev Immunol* 2021;21: 739-51.
- Perkin MR, Strachan DP. The hygiene hypothesis for allergy - conception and evolution. *Front Allergy* 2022;3:1051368.
- Muhammad Danial Song HJJ, Min Lee CT, Ci Ng FY, Jyn Tan BK, Ho Siah KT, Tham EH. Childhood acid suppressants may increase allergy risk-a systematic review and meta-analysis. *J Allergy Clin Immunol Pract* 2023;11: 228-37.e8.

24. Fleischer DM, Chan ES, Venter C, Spergel JM, Abrams EM, Stukus D, et al. A consensus approach to the primary prevention of food allergy through nutrition: guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology. *J Allergy Clin Immunol Pract* 2021;9:22-43.e4.
25. Turner PJ, Feeny M, Meyer R, Perkin MR, Fox AT. Implementing primary prevention of food allergy in infants: new BSACI guidance published. *Clin Exp Allergy* 2018;48:912-5.
26. Joshi PA, Smith J, Vale S, Campbell DE. The Australasian Society of Clinical Immunology and Allergy infant feeding for allergy prevention guidelines. *Med J Aust* 2019;210:89-93.
27. Halken S, Muraro A, de Silva D, Khaleva E, Angier E, Arasi S, et al. EAACI guideline: preventing the development of food allergy in infants and young children (2020 update). *Pediatr Allergy Immunol* 2021;32:843-58.
28. Tham EH, Shek LP, Van Bever HP, Vichyanond P, Ebisawa M, Wong GW, et al. Early introduction of allergenic foods for the prevention of food allergy from an Asian perspective-an Asia Pacific Association of Pediatric Allergy, Respiriology & Immunology (APAPARI) consensus statement. *Pediatr Allergy Immunol* 2018;29:18-27.
29. Ebisawa M, Ito K, Fujisawa T, Aihara Y, Imai T, Ito S, et al. Japanese guidelines for food allergy 2020. *Allergol Int* 2020;69:370-86.
30. Tham EH, Leung ASY, Yamamoto-Hanada K, Dahdah L, Trikamjee T, Warad VV, et al. A systematic review of quality and consistency of clinical practice guidelines on the primary prevention of food allergy and atopic dermatitis. *World Allergy Organ J* 2023;16:100770.
31. Sicherer SH, Burks AW. Maternal and infant diets for prevention of allergic diseases: understanding menu changes in 2008. *J Allergy Clin Immunol* 2008;122:29-33.
32. Greer FR, Sicherer SH, Burks AW. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics* 2008;121:183-91.
33. Du Toit G, Katz Y, Sasieni P, Meshher D, Maleki SJ, Fisher HR, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008;122:984-91.
34. Dietary Guidelines for Americans, 2020-2025; 2020. Accessed September 3, 2025. Available from: <https://www.dietaryguidelines.gov/>
35. Puri S, Anumakonda V. East meets West: navigating the health challenges of shifting from traditional to Western diets. *Recent Adv Clin Trials* 2024;4:1-4.
36. Yamamoto-Hanada K, Pak K, Saito-Abe M, Yang L, Sato M, Irahara M, et al. Allergy and immunology in young children of Japan: the JECS cohort. *World Allergy Organ J* 2020;13:100479.
37. Ooraikul B, Sirichote A, Siripongvutikorn S. Southeast Asian diets and health promotion. In: Meester F, Watson RR, editors. *Wild-type food in health promotion and disease prevention: the Columbus concept*. Springer; 2008. p. 515-33.
38. Kabeer S, Mary SJ, Govindarajan N, Essa MM, Qoronfleh MW. Traditional weaning foods and processing methods with fortification for sustainable development of infants to combat zero hunger: a review. *J Food Sci Technol* 2024;61:2263-74.
39. Soriano VX, Peters RL, Moreno-Betancur M, Ponsonby AL, Gell G, Odoi A, et al. Association between earlier introduction of peanut and prevalence of peanut allergy in infants in Australia. *JAMA* 2022;328:48-56.
40. Netting MJ, Moumin NA, Makrides M, Green TJ. The Australian Feeding Infants and Toddlers Study (OzFITS) 2021: highlights and future directions. *Nutrients* 2022;14:4343.
41. Harama D, Saito-Abe M, Hamaguchi S, Fukuie T, Ohya Y, Yamamoto-Hanada K. Feasibility and safety of the early introduction of allergenic foods in Asian infants with eczema. *Nutrients* 2024;16:1578.
42. Perkin MR, Logan K, Tseng A, Raji B, Ayis S, Peacock J, et al. Randomized trial of introduction of allergenic foods in breast-fed infants. *N Engl J Med* 2016;374:1733-43.
43. Kjellman NI, Johansson S. Soy versus cow's milk in infants with a biparental history of atopic disease: development of atopic disease and immunoglobulins from birth to 4 years of age. *Clin Exp Allergy* 1979;9:347-58.
44. Lowe AJ, Hosking CS, Bennett CM, Allen KJ, Axelrad C, Carlin JB, et al. Effect of a partially hydrolyzed whey infant formula at weaning on risk of allergic disease in high-risk children: a randomized controlled trial. *J Allergy Clin Immunol* 2011;128:360-5.e4.
45. Urashima M, Mezawa H, Okuyama M, Urashima T, Hirano D, Gocho N, et al. Primary prevention of cow's milk sensitization and food allergy by avoiding supplementation with cow's milk formula at birth: a randomized clinical trial. *JAMA Pediatr* 2019;173:1137-45.
46. Bellach J, Schwarz V, Ahrens B, Trendelenburg V, Aksamit Ö, Kalb B, et al. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants. *J Allergy Clin Immunol* 2017;139:1591-9.e2.
47. Iannotti LL, Lutter CK, Stewart CP, Gallegos Riofrío CA, Malo C, Reinhart G, et al. Eggs in early complementary feeding and child growth: a randomized controlled trial. *Pediatrics* 2017;140:e20163459.
48. Palmer DJ, Metcalfe J, Makrides M, Gold MS, Quinn P, West CE, et al. Early regular egg exposure in infants with eczema: a randomized controlled trial. *J Allergy Clin Immunol* 2013;132:387-92.e1.
49. Palmer DJ, Sullivan TR, Gold MS, Prescott SL, Makrides M. Randomized controlled trial of early regular egg intake to prevent egg allergy. *J Allergy Clin Immunol* 2017;139:1600-7.e2.
50. Wei-Liang Tan J, Valerio C, Barnes EH, Turner PJ, Van Asperen PA, Kakakios AM, et al. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. *J Allergy Clin Immunol* 2017;139:1621-8.e8.
51. Scarpone R, Kimkool P, Ierodiakonou D, Leonardi-Bee J, Garcia-Larsen V, Perkin MR, et al. Timing of allergenic food introduction and risk of immunoglobulin E-mediated food allergy: a systematic review and meta-analysis. *JAMA Pediatr* 2023;177:489-97.
52. Katz Y, Rajuan N, Goldberg MR, Eisenberg E, Heyman E, Cohen A, et al. Early exposure to cow's milk protein is protective against IgE-mediated cow's milk protein allergy. *J Allergy Clin Immunol* 2010;126:77-82.e1.
53. Kojima R, Shinohara R, Kushima M, Yui H, Otawa S, Horiuchi S, et al. Infantile peanut introduction and peanut allergy in regions with a low prevalence of peanut allergy: the Japan Environment and Children's Study (JECS). *J Epidemiol* 2024;34:324-30.
54. NTT Data Institute of Management Consulting. TOKACHI Grand Nuts Project: Implementing High Value-Added Agriculture Centered on Peanuts and Creating Regional Value Chains; 2017. Accessed September 3, 2025. Available from: [https://www.nttdata-strategy.com/newsrelease/archives/170828/?utm\\_source=chatgpt.com](https://www.nttdata-strategy.com/newsrelease/archives/170828/?utm_source=chatgpt.com)
55. Yamamoto-Hanada K, Ohya Y. Management of infant atopic eczema to prevent severe eczema and food allergy. *Clin Exp Allergy* 2024;54:669-81.
56. Miyaji Y, Yang L, Yamamoto-Hanada K, Narita M, Saito H, Ohya Y. Earlier aggressive treatment to shorten the duration of eczema in infants resulted in fewer food allergies at 2 years of age. *J Allergy Clin Immunol Pract* 2020;8:1721-4.e6.
57. Yamamoto-Hanada K, Kobayashi T, Williams HC, Mikami M, Saito-Abe M, Morita K, et al. Early aggressive intervention for infantile atopic dermatitis to prevent development of food allergy: a multicenter, investigator-blinded, randomized, parallel group controlled trial (PACI Study)-protocol for a randomized controlled trial. *Clin Transl Allergy* 2018;8:47.
58. Kumagai F, Yamamoto-Hanada K, Saito-Abe M, Sato M, Ishikawa F, Irahara M, et al. FLG mutations, eczema control, and respiratory symptom at one-year-old in early-onset atopic dermatitis infants (PACI-ON cohort study). *J Dermatol Sci* 2023;109:99-101.
59. US National Library of Medicine, Seal, Stopping Eczema and Allergy Study. Accessed September 3, 2025. Available from: <https://clinicaltrials.gov/ct2/show/NCT03742414>
60. Yamamoto-Hanada K, Okamoto K, Kishimoto N, Tsuchiya K, Natsume O, Takemura Y, et al. DIFENSE study protocol: early intervention with difamylast ointment in infantile early-onset atopic dermatitis for prevention of transcutaneous sensitization. *Clin Exp Allergy* 2025;55:580-2.
61. Zhong Y, Samuel M, van Bever H, Tham EH. Emollients in infancy to prevent atopic dermatitis: a systematic review and meta-analysis. *Allergy* 2022;77:1685-99.
62. Kelleher MM, Phillips R, Brown SJ, Cro S, Cornelius V, Carlsen KCL, et al. Skin care interventions in infants for preventing eczema and food allergy. *Cochrane Database Syst Rev* 2022;11:C0013534.
63. Tham EH, Yamamoto-Hanada K, Leung ASY, Ohya Y. Role of skin management in the prevention of atopic dermatitis and food allergy. *Pediatr Allergy Immunol* 2024;35:e14094.
64. Tsilochristou O, du Toit G, Sayre PH, Roberts G, Lawson K, Sever ML, et al. Association of *Staphylococcus aureus* colonization with food allergy occurs independently of eczema severity. *J Allergy Clin Immunol* 2019;144:494-503.
65. Martin P, Eckert J, Koplin J, Lowe A, Gurrin L, Dharmage S, et al. Which infants with eczema are at risk of food allergy? Results from a population-based cohort. *Clin Exp Allergy* 2015;45:255-64.
66. Shoda T, Futamura M, Yang L, Yamamoto-Hanada K, Narita M, Saito H, et al. Timing of eczema onset and risk of food allergy at 3 years of age: a hospital-based prospective birth cohort study. *J Dermatol Sci* 2016;84:144-8.

67. Wong JJ, Margolis DJ. Association between food allergy status and atopic dermatitis control and persistence: a longitudinal analysis of the Pediatric Eczema Elective Registry. *Pediatr Dermatol* 2025;42:552-5.
68. Yamamoto-Hanada K, Suzuki Y, Yang L, Saito-Abe M, Sato M, Mezawa H, et al. Persistent eczema leads to both impaired growth and food allergy: JECs birth cohort. *PLoS One* 2021;16:e0260447.
69. Lopes JP, Cox AL, Baker MG, Bunyavanich S, Oriol RC, Sicherer SH, et al. Peanut-induced food protein-induced enterocolitis syndrome (FPIES) in infants with early peanut introduction. *J Allergy Clin Immunol Pract* 2021;9:2117-9.
70. Hill DJ, Hosking CS, de Benedictis FM, Oranje AP, Diepgen TL, Bauchau V. Confirmation of the association between high levels of immunoglobulin E food sensitization and eczema in infancy: an international study. *Clin Exp Allergy* 2008;38:161-8.
71. Fukuie T, Nomura I, Horimukai K, Manki A, Masuko I, Futamura M, et al. Proactive treatment appears to decrease serum immunoglobulin-E levels in patients with severe atopic dermatitis. *Br J Dermatol* 2010;163:1127-9.
72. Fukuie T, Hirakawa S, Narita M, Nomura I, Matsumoto K, Tokura Y, et al. Potential preventive effects of proactive therapy on sensitization in moderate to severe childhood atopic dermatitis: a randomized, investigator-blinded, controlled study. *J Dermatol* 2016;43:1283-92.
73. Fukuie T, Nishiura H, Miyaji Y, Matsumoto K, Ohya Y, Saito H. Effect of specific IgE on eliciting dose in children with cow's milk allergy. *J Allergy Clin Immunol Pract* 2020;8:3660-2.e2.
74. Peters RL, Allen KJ, Dharmage SC, Tang ML, Koplin JJ, Ponsonby AL, et al. Skin prick test responses and allergen-specific IgE levels as predictors of peanut, egg, and sesame allergy in infants. *J Allergy Clin Immunol* 2013;132:874-80.
75. Lachover-Roth I, Cohen-Engler A, Furman Y, Shachar I, Rosman Y, Meir-Shafir K, et al. Early, continuing exposure to cow's milk formula and cow's milk allergy: the COMEET study, a single center, prospective interventional study. *Ann Allergy Asthma Immunol* 2023;130:233-9.e4.
76. Sakihara T, Otsuji K, Arakaki Y, Hamada K, Sugiura S, Ito K. Early discontinuation of cow's milk protein ingestion is associated with the development of cow's milk allergy. *J Allergy Clin Immunol Pract* 2022;10:172-9.
77. Wai-Yan Leong O, Perrett KP, Loke P, Koplin JJ, Tang MLK, Allen KJ, et al. Reintroduction of peanut into the infant diet following negative peanut oral food challenges. *J Allergy Clin Immunol Pract* 2024;12:779-82.e1.
78. Wen X, Martone GM, Lehman HK, Rideout TC, Cameron CE, Dashley S, et al. Frequency of infant egg consumption and risk of maternal-reported egg allergy at 6 years. *J Nutr* 2023;153:364-72.
79. Abrams EM, Orkin J, Cummings C, Blair B, Chan ES. Dietary exposures and allergy prevention in high-risk infants. *Paediatr Child Health* 2021;26:504-5.
80. Takada K, Fukuie T, Ogita H, Hirai S, Toyokuni K, Yamamoto-Hanada K, et al. Quantitative risk assessment of egg-white, milk and wheat in infants. *Allergy* 2024;79:533-6.
81. Groetch M, Mudd K, Woch M, Schaible A, Gray BE, Babineau DC, et al. Retail food equivalents for post-oral immunotherapy dosing in the omalizumab as monotherapy and as adjunct therapy to multi-allergen oral immunotherapy in food-allergic children and adults (OUTMATCH) Clinical Trial. *J Allergy Clin Immunol Pract* 2023;11:572-80.e2.
82. US Department of Agriculture. Food Data Central. Accessed September 3, 2025. <https://fdc.nal.usda.gov/food-details/2661133/nutrients>
83. World Health Organization. Risk assessment of food allergens. Part 2: review and establish threshold levels in foods for the priority allergens; 2023. Meeting Report. Accessed September 3, 2025. Available from: <https://www.who.int/publications/i/item/9789240065420>
84. Hamaguchi S, Harama D, Saito-Abe M, Ishikawa F, Sato M, Fukuie T, et al. Evaluation of commercial early introduction products in infants: protein content of early introduction products. *Clin Exp Allergy* 2024;54:939-42.
85. Cox AL, Shah A, Groetch M, Sicherer SH. Allergic reactions in infants using commercial early allergen introduction products. *J Allergy Clin Immunol Pract* 2021;9:3517-20.e1.
86. Koplin JJ, Peters RL, Ponsonby A-L, Gurrin LC, Hill D, Tang MLK, et al. Increased risk of peanut allergy in infants of Asian-born parents compared to those of Australian-born parents. *Allergy* 2014;69:1639-47.
87. Soriano VX, Allen KJ, Dharmage SC, Shifti DM, Perrett KP, Wijesuriya R, et al. Prevalence and determinants of food allergy in the era of early allergen introduction: the EarlyNuts population-based study. *J Allergy Clin Immunol Pract* 2024;12:3068-78.e3.
88. Jiang J, Warren CM, Brewer A, Soffer G, Gupta RS. Racial, ethnic, and socioeconomic differences in food allergies in the US. *JAMA Netw Open* 2023;6:e2318162.
89. Hamaguchi S, Saito-Abe M, Fukuie T, Ohya Y, Yamamoto-Hanada K. Does appropriate timing for early introduction differ between hen's eggs and nuts? *Clin Exp Allergy* 2024;54:700-2.
90. Peters RL, Barret DY, Soriano VX, McWilliam V, Lowe AJ, Ponsonby A-L, et al. No cashew allergy in infants introduced to cashew by age 1 year. *J Allergy Clin Immunol* 2021;147:383-4.
91. Gibson V, Ullman A, Takashima M, Koplin J. Barriers and enablers of dietary reintroduction following negative oral food challenge: a scoping review. *J Allergy Clin Immunol Pract* 2025;13:851-60.e7.
92. Inuzuka Y, Yamamoto-Hanada K, Akaishi R, Haruna M, Matsubara M, Saito-Abe M, et al. Dissemination of atopic dermatitis and food allergy information to pregnant women in an online childbirth preparation class. *J Allergy Clin Immunol Glob* 2022;1:24-6.
93. Yamamoto-Hanada K, Takayama JI, Saito-Abe M, Futamura M, Ohya Y. Prenatal visits for allergy prevention. *Ann Allergy Asthma Immunol* 2020;124:198-200.
94. Wang J, Bird JA, Cleary K, Doucette J, du Toit G, Groetch M, et al. Awareness and application of United States Food Allergy Prevention Guidelines among pediatricians and other clinicians. *J Pediatr* 2024;275:114218.