

The Epidemiology of Food Allergy

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Abstract

Purpose of Review The past few years have seen an exponential increase in publications on the topic of IgE-mediated food allergy. Recent publications have greatly advanced our understanding of the global prevalence of food allergy, and have revealed new insights into risk factors for food allergy. In this article, we will review these recent developments, summarise the current state of knowledge of the epidemiology of IgE-mediated food allergy, and outline areas of ongoing research where gaps in evidence remain.

Recent Findings Recent publications reveal substantial differences in food allergy prevalence between countries. Data show that the incidence of food-induced anaphylaxis in developed countries continues to rise, particularly in children, although it remains unclear to what extent this is due to an increase in food allergy prevalence, or an increase in severe reactions among allergic individuals, or both. There has been considerable progress in understanding risk factors for food allergy. In particular, there is now good evidence that delayed introduction of peanut increases the risk of developing peanut allergy in infants with pre-existing risk factors for peanut allergy. A shift towards earlier introduction of peanut in these infants, now starting to be recommended in allergy prevention

guidelines, may help to prevent peanut allergy in future generations.

Summary Recent studies have defined the prevalence of food allergy in different regions of the world. These studies provide strong baseline data to measure the extent to which new food allergy prevention strategies, including recommending timely peanut introduction for high-risk infants, change the prevalence of childhood food allergy.

Keywords Food allergy · Peanut allergy · Egg allergy · Prevalence · Risk factors · Epidemiology

Introduction

Allergic diseases—asthma, hay fever, eczema and IgE-mediated food allergy—are now widely recognised as an important public health burden in developed countries. While all these conditions are to some extent interrelated, sharing some common mechanisms and potentially co-existing within individuals, they differ in natural history, prevalence and time trends. Collectively, these differences suggest that the increase in food allergy may have distinct and unique drivers.

Food allergy often manifests in infancy when new foods are introduced into an infants' diet. Symptoms of IgE-mediated food allergy include hives, angioedema (swelling) of the face or lips, vomiting and (less commonly) anaphylaxis, a life-threatening allergic reaction that may involve the airways or circulatory system, and these symptoms develop rapidly following exposure to the food [1]. The prevalence of food allergy in infants and young children (discussed in detail in following sections) is estimated to be around 5–10 %. By contrast, eczema—which also often begins in infancy—may affect more than 20 %

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of infants [2]. Asthma and allergic rhinitis generally begin later in childhood.

Intriguingly, a rise in food allergy prevalence appears to have occurred at least one generation after the rise in prevalence of allergic rhinitis and asthma [3]. Perhaps as a result of this, research into food allergy has lagged behind research into other childhood allergic diseases, and as recently as 10 years ago there were major gaps in knowledge about the epidemiology of food allergy. Since then, progress has been rapid and the past few years have seen important advances in our understanding of food allergy prevalence, mechanisms and risk factors. This review will discuss recent advances in understanding the epidemiology of IgE-mediated food allergy, with a particular focus on new insights from the past 3 years.

Increasing Incidence of Food Allergy-Induced Anaphylaxis

Studies from various regions of the world have shown an increasing incidence of hospital admissions for food-induced anaphylaxis, particularly in young children, although it remains unclear to what extent this is due to a true increase in prevalence of food allergy, an increase in severe reactions among allergic individuals, or both. Emergency department visits and hospital admissions for food-induced anaphylaxis more than doubled in US children from 2000 to 2009 [4] and increased fivefold in Italian children over a 10-year period from 2001 to 2011 [5]. A similar magnitude of increase was seen in Australian children over a similar time period, with a fivefold increase in admissions in the under 5 year age group between 1995 and 2005 [6]. Interestingly, between 1995 and 2005, the most rapid increase in food-induced anaphylaxis was seen in the 0–4 year age group, while in more recent years (2006–2012) there has been an accelerating rate of increase in the 5–14 year age group, suggesting an increasing burden in older age groups (who carry a higher risk for fatal anaphylaxis) as this cohort of children grows up [7•].

Despite increases in food-induced anaphylaxis hospital admissions from the early 1990s to the 2010s in the US, UK and Australia, an increase in fatalities was only noted in Australia (9.7 % per year, 95 % CI 0.25–20 %, between 1997 and 2013) [6, 8•, 9, 10]. Over the 16-year period studied, there were 23 recorded cases of fatal food anaphylaxis in Australia [10]. A lack of increase in fatalities in other countries despite an increase in admissions could be explained by improved treatment of anaphylaxis episodes reducing the risk of fatal outcomes. Alternatively, it is possible that improved recognition, coding (in hospital databases) and awareness of anaphylaxis led to an increase in cases of anaphylaxis either presenting to the hospital or

being captured in hospital databases without a real increase in the incidence of this condition.

It is difficult to draw conclusions about any changes in the prevalence of food allergy based on the incidence of hospital admissions for food-induced anaphylaxis, since any increase in this measure could be due to a number of factors. There are many different drivers of hospital presentations for anaphylaxis, both regional and personal, making it difficult to understand whether hospital presentations are an accurate surrogate marker of overall rates of anaphylaxis. Other data sources are therefore required to examine the population prevalence of food allergy.

Recent Insights into the Global Prevalence of Food Allergy

Understanding the prevalence of food allergy in different regions in the world is vital for allergy workforce planning and for tracking changes in allergy prevalence over time to measure the impact of food allergy prevention strategies as these begin to be implemented. Measuring differences in prevalence between countries and in different regions within countries also has the potential to provide important insights into risk factors and drivers of food allergy. As such, it is exciting to see new studies emerge measuring food allergy prevalence in previously understudied regions of the world. Recent publications have greatly advanced our understanding of the global prevalence of food allergy, and have revealed substantial differences in prevalence between countries.

In the past, attempts to compare the prevalence of food allergy between different countries and regions had been complicated by inconsistent definitions of food allergy and non-standardised study design. Most studies used self- or parent-reported food allergy outcomes, which usually overestimates the true prevalence of food allergy because food intolerances and other non-IgE-mediated reactions are incorrectly attributed to IgE-mediated food allergy [1]. Even doctor-diagnosed food allergy has limitations, particularly when comparing estimates from different countries or regions, since lack of awareness of food allergies and less access to health care in some regions can lead to an artificially lower prevalence of doctor-diagnosed food allergy. Double-blind placebo-controlled food challenges (DBPCFC) are regarded as the gold standard for diagnosing food allergy, with open food challenges also acceptable in infants or when symptoms are objective immediate type reactions [1, 11].

Several recent studies have now measured the prevalence of food allergy using oral food challenges to confirm allergy, with many of these studies conducted in infants and young children. Infancy is an important and previously

understudied age group since many IgE-mediated food allergies present when foods are introduced into the infant diet for the first time, often in the first year of life. It is also important to define the current prevalence of food allergy in infants and young children since this is thought to have increased in recent generations, thus food allergy prevalence in the latest generation of infants may be quite different to past estimates. Global estimates of food allergy prevalence measured by oral food challenge are summarised in Fig. 1 and Table 1. Since food allergy prevalence varies with age, making it difficult to compare between studies conducted in different age groups, we restricted this figure to only studies including infants and children under 2 years of age.

Recent publications from the EuroPrevall consortium have gone some way towards resolving previous issues related to non-standardised study design and suboptimal measurements of food allergy outcomes [12•, 13•]. The EuroPrevall birth cohort study was designed to compare food allergy prevalence between countries by using a standardised study protocol, including oral food challenges to diagnose food allergy, in multiple European centres. Around 12,000 infants from nine countries were recruited into a series of birth cohorts in 2005–2010, with approximately 9000 infants followed up to 2 years of age. Infants with eczema or suspected food allergy reported at telephone interview at 12 and 24 months of age were invited for clinical testing, including measurement of specific IgE levels in serum (sIgE) and/or skin prick testing (SPT) and, if warranted based on symptoms or SPT/sIgE results, DBPCFC. Participation rates varied between centres, and were not recorded for all centres, thus it is not completely clear how well the reported prevalence of food allergy in each centre represents the true prevalence in the wider population of infants in that region [14]. Despite this, for many countries the data from EuroPrevall represent the best available measurement of food allergy in European infants. Adjusted prevalence figures were calculated, which assign a “likely allergy” status to infants who declined food challenge (approximately 40 % of the cohort). Overall, adjusted IgE-mediated cow’s milk allergy prevalence in Europe in the first 2 years of life was 0.59 % (95 % CI 0.43–0.80) [12•], and egg allergy was 1.23 % (95 % CI 0.98–1.51) [13•].

Outside of Europe, the HealthNuts study in Australia recruited 12 month old infants around the same time as EuroPrevall. Infants were recruited between 2007 and 2011 from council-led immunisation sessions throughout Melbourne, Australia, with 74 % of eligible infants participating in the study. All infants underwent skin prick testing to detect the presence of IgE antibodies to egg, peanut and sesame, and those positive had an oral food challenge to determine clinical allergy status (83 % participated in food challenges).

Of the 5300 participating infants, 3 % were peanut allergic, 9 % egg allergic and 0.8 % sesame allergic [15, 16].

Recently, there have been new publications reporting the prevalence of food allergy in infants in South Africa and China, both countries where food allergy was previously considered to be rare. The South African Food Sensitisation and Food Allergy study (SAFFA) used a population-based sampling frame to recruit an unselected cohort of infants in Cape Town, South Africa [17]. Children aged 12–36 months were recruited from childcare centres (60.1 % response rate). All infants underwent skin prick testing, and those with any level of sensitisation underwent an oral food challenge unless they had clear history of tolerance to that food. In an interim analysis of the first 544 participants, the prevalence of challenge-proven IgE-mediated allergy was 2.5 % (95 % CI 1.2–3.9), with a 1.8 % prevalence of allergy to egg, 1.2 % to peanut and 0.2 % to cow’s milk. A study in Chongqing, China, recruited 497 infants from nine districts of Chongqing attending the Children’s Hospital of Chongqing Medical University for routine health checks, with a participation rate of 96 % (477/497) [18]. Parents completed a questionnaire and all participating subjects underwent skin prick testing. Children with positive SPT results or a history of parent-reported adverse reaction to foods underwent oral food challenges. The prevalence of challenge-proven food allergy was 3.8 % (95 % CI 2.5–5.9), with a 2.5 % prevalence of egg allergy and 1.3 % to cow’s milk. Only two infants (0.4 %) were sensitised to peanut and one to fish and shrimp, and there were no positive challenges to peanut, fish or shrimp.

These recent studies have shown fairly large differences in infant food allergy prevalence between countries, with Australia having the highest recorded prevalence. The prevalence of food allergy in countries where food allergy was previously thought to be uncommon such as China and South Africa was similar to the prevalence recorded in Europe, suggesting that rises in food allergy might be occurring globally. Factors contributing to these between-country differences are incompletely understood, although there are several hypotheses and these are discussed in subsequent sections of this review.

Time Trends in Food Allergy Prevalence

High-quality time trend data for food allergy are still lacking from most countries, thus the magnitude of any increase in food allergy prevalence in different regions of the world is unclear. There are few studies comparing the prevalence of challenge-confirmed food allergy in the same population at different times, although the studies that do exist suggest an increasing prevalence. A series of three cohort studies on the Isle of Wight in the UK over a

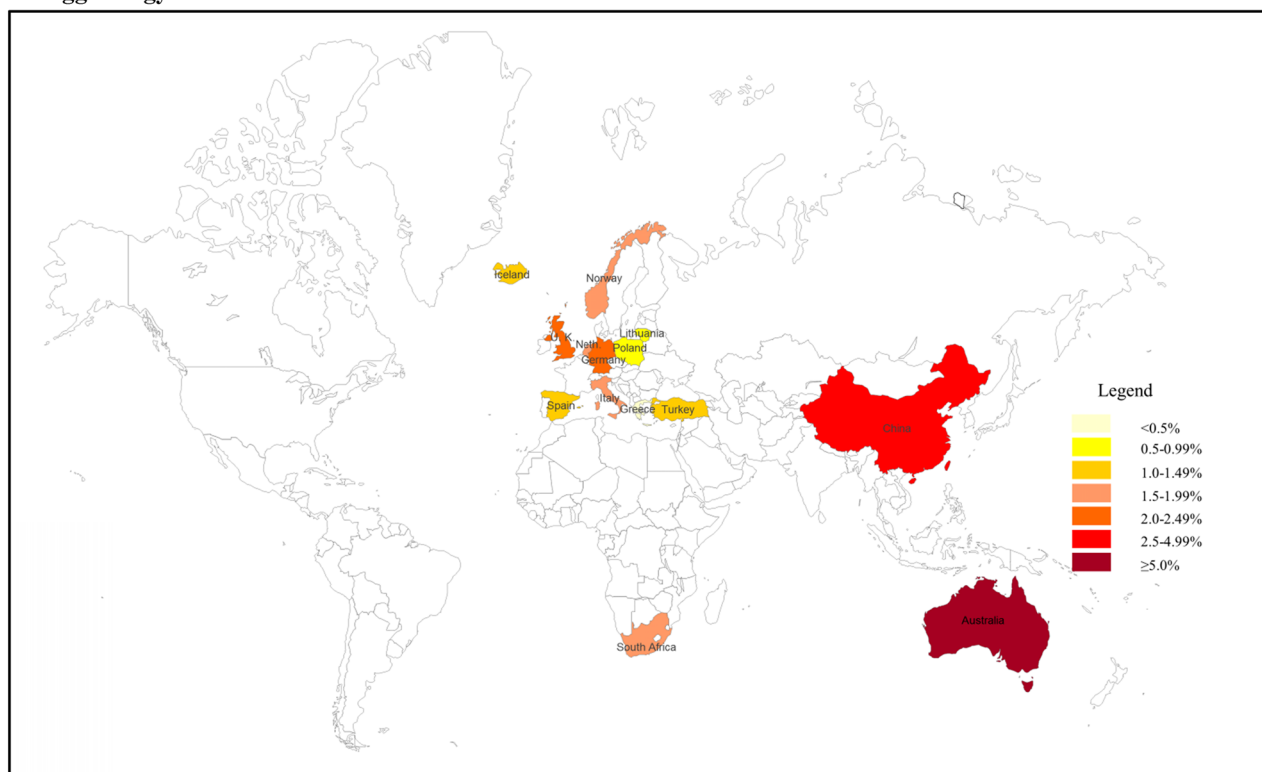
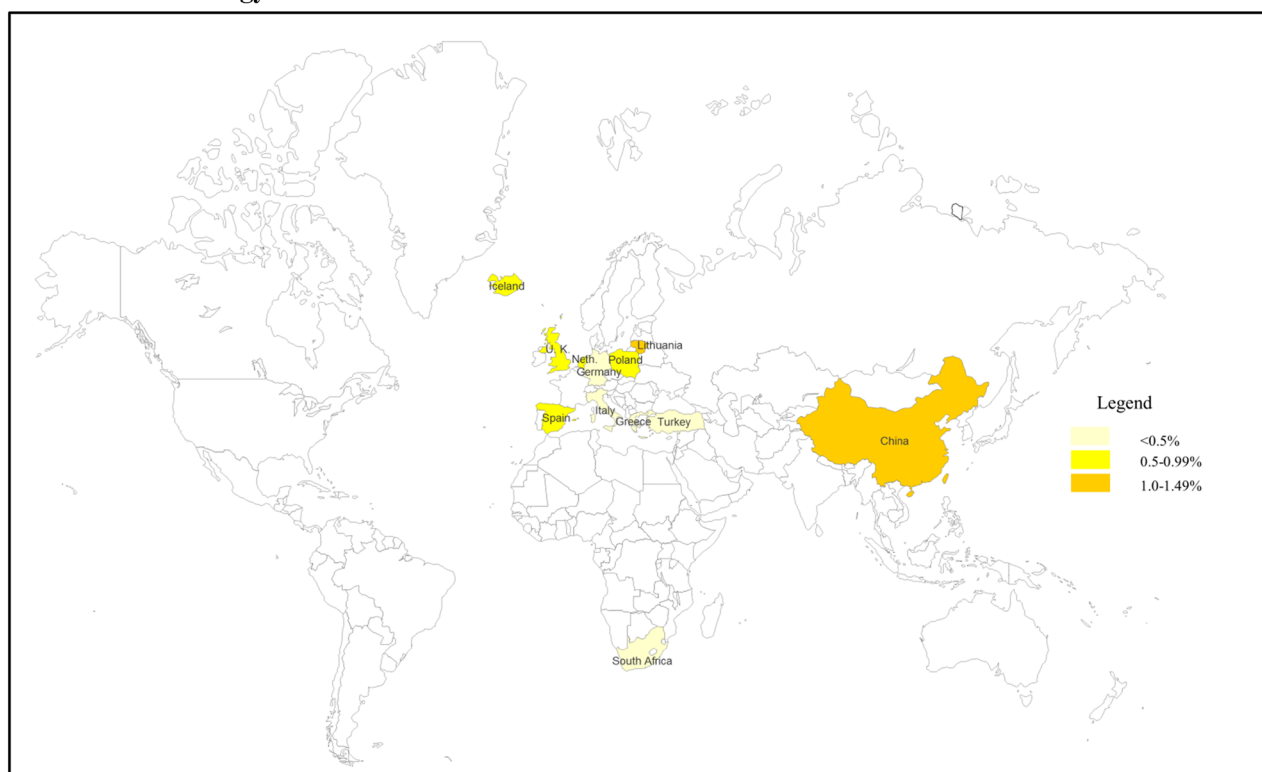
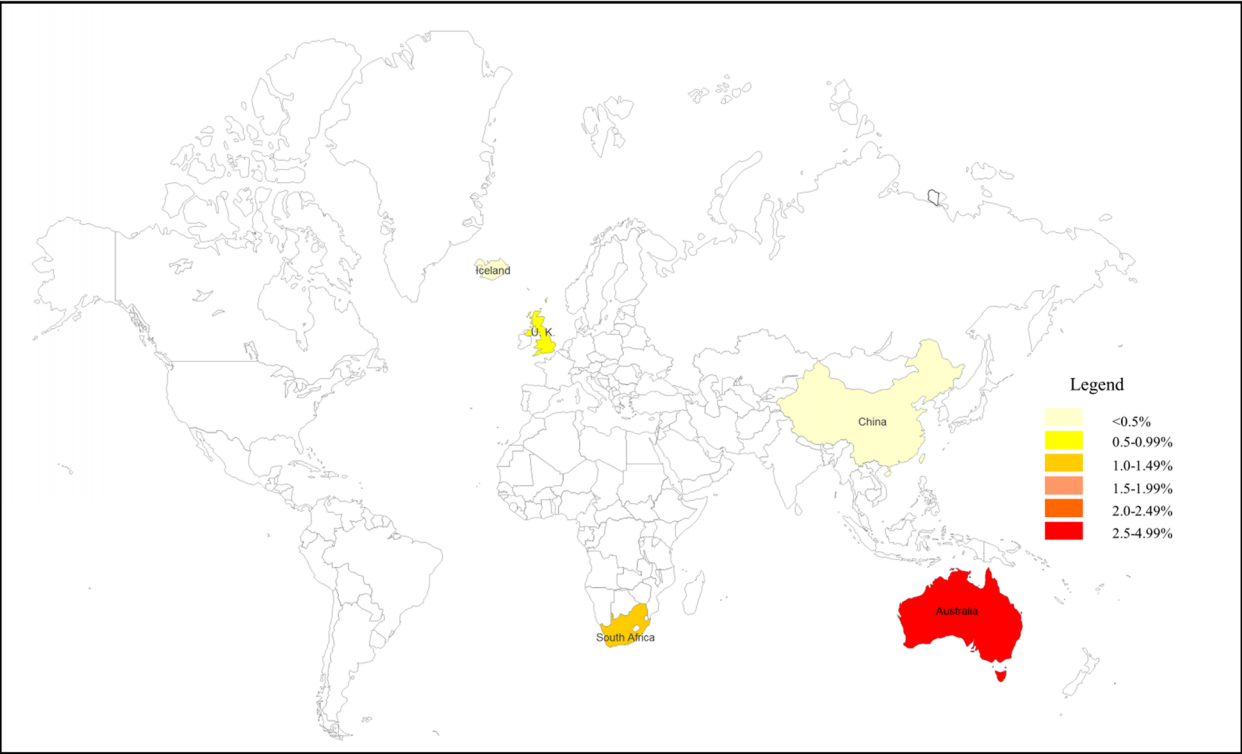
A Egg allergy**B Cow's milk allergy**

Fig. 1 Studies reporting the prevalence of challenge-proven IgE-mediated food allergy in infants and young children. **a** Egg allergy; **b** Cow's milk allergy; **c** Peanut allergy; **d** Overall food allergy prevalence (Color figure online)

C Peanut allergy



D Overall food allergy

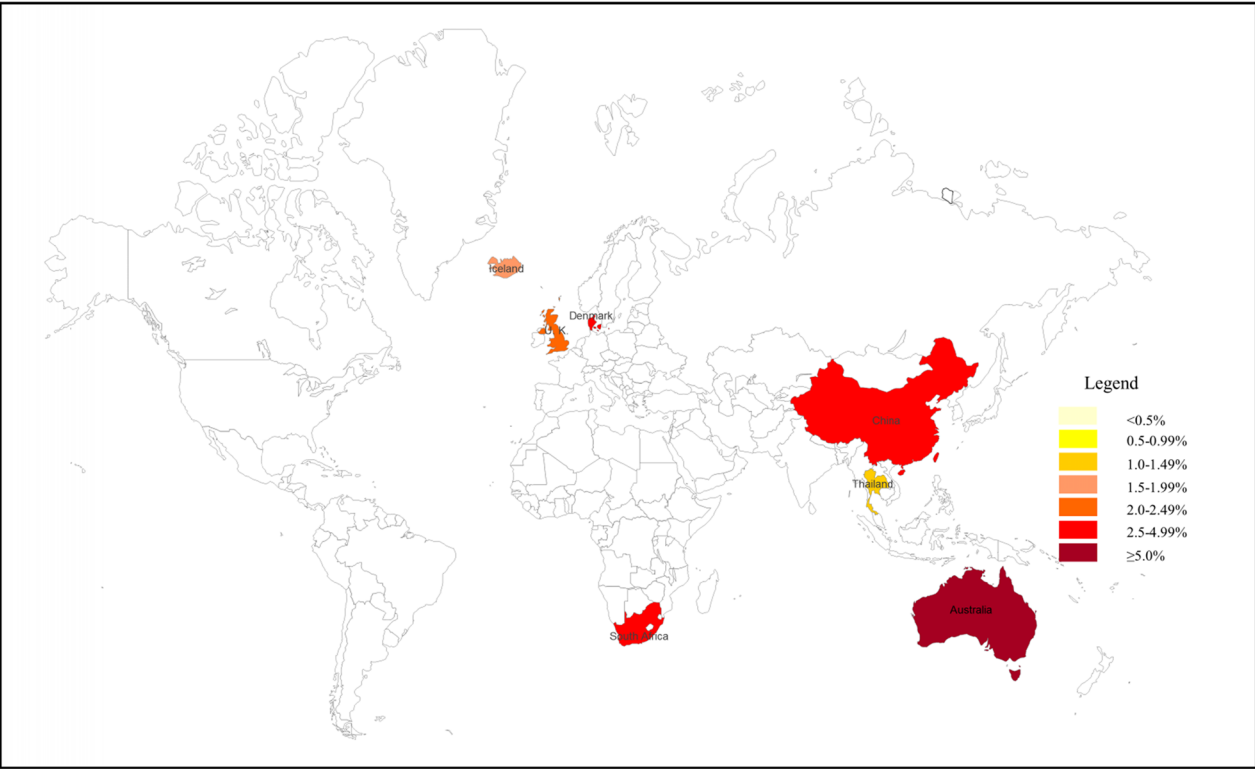


Fig. 1 continued

10-year period showed an increase in peanut sensitisation and peanut allergy in 3–4 year old children between 1993 and 1997–2000, but no further increase in 2004 [19]. Two small cross-sectional studies in Chongqing, China showed an increase in food sensitisation and allergy prevalence in 0–24 month old infants between 1999 and 2009 [20]. Reasons for these changes were not examined.

Further time trend data are required to capture the more recent changes in food allergy prevalence. The recent studies measuring challenge-confirmed food allergy prevalence across Europe, in Australia, China and South Africa, described above, have provided strong baseline prevalence data. This is a vital first step to measuring changes in food allergy prevalence in the future. Importantly, these baseline data will allow us to measure the extent to which new interventions, including a shift towards earlier introduction of dietary peanut and other allergenic foods, alter the prevalence of food allergy.

Which Foods Are the Most Common Triggers for IgE-Mediated Food Allergy?

Although many foods have been reported as triggers of food allergy, the foods or food groups commonly associated with IgE-mediated food allergy are cow's milk, egg, peanut, tree nuts and seeds, soy, wheat, fish and shellfish [1]. The prevalence of these different types of food allergies varies by age group due to their differing natural history. Allergies to egg, milk and nut generally develop in infancy, with egg and milk allergy often being rapidly outgrown and nut allergies usually persisting into later life, while allergies to shellfish may only develop later in childhood or adolescence.

Recent studies have provided new insights into the relative frequency of these allergies in the infant population. As described above, egg allergy was consistently found to be the most common IgE-mediated food allergy in the infant population in Europe, Australia, China and South Africa. In the EuroPrevall studies, egg allergy was approximately twice as common as cow's milk allergy. Both cow's milk allergy and egg allergy in infants are often transient, with approximately 50 % of infants outgrowing their egg allergy within 1 year in both the EuroPrevall and HealthNuts studies [13•, 21] and two-thirds outgrowing their cow's milk allergy within a year [12•].

Peanut allergy has been the most studied food allergy and a cause of significant community and clinical concern. Compared with egg and milk allergy, it is less often outgrown and is more often associated with anaphylaxis [22]. In the HealthNuts and SAFFA studies, peanut allergy was more common at one year of age than cow's milk allergy, although less common than egg allergy [15–17].

HealthNuts also provided longitudinal data on peanut allergy. At age 1 year, 3 % of children were peanut allergic, with around 20 % of these children outgrowing their allergy by age 4 years [23•]. This finding is consistent with previous clinical cohort studies showing resolution of peanut allergy during childhood in 20 % of allergic patients [24].

Along with peanut, tree nut allergy has also been implicated as a common cause of severe allergic reactions including deaths [8•]. Despite this, a recent systematic review found that the prevalence of tree nut allergy has not been well characterised, with most existing studies limited to self-reported data [25•]. There were also limited data on which tree nuts are the most common triggers of food allergy in different countries. Hazelnut has been reported as a common trigger of tree nut allergy in Europe, walnut and cashew in the US and a range of nuts including almond, Brazil nut and walnut in the UK. A potential explanation for relatively high rates of hazelnut allergy in some regions of Europe is the presence of oral allergy syndrome, also known as birch pollen food syndrome, in these regions. This syndrome occurs when individuals with sensitisation to birch pollen have IgE antibodies that cross-react with similar proteins found in hazelnut, resulting in oral pharyngeal symptoms.

New Insights from Migration Studies

Two recent population-based food allergy studies showed that parental migration from Asia to Australia greatly increased the risk of food allergy in the next generation, born in Australia. In the population-based HealthNuts study, challenge-confirmed food allergy was three times more common in infants with parents born in East Asia compared to those with parents born in Australia [26]. Similar effects were seen for eczema [2]. The increased risk of allergic disease in Australian-born infants of Asian-born parents appears to have occurred in a single generation, with the prevalence of reported allergic disease similar or even lower in Asian-born parents themselves compared with Australian-born parents. Furthermore, the increased risk appeared to be specific to infants of Asian parents and was not seen among infants of parents born in the UK or Europe. A separate cohort in Victoria confirmed this finding and additionally found that children born in Asia who subsequently migrate to Australia in childhood are protected against food allergy [27] (Fig. 2).

Collectively, these migration findings suggest that environmental exposures occurring either in utero or very early in life are crucial in determining the risk of food allergy. Differences in environmental exposures between the parent and offspring might also be an important factor in this phenomenon.

Table 1 Prevalence of challenge-proven IgE-mediated food allergy in infants and young children

Country	Age group	N	Prevalence (%) (95 % CI) ^a				
			Egg allergy	Cow's milk allergy	Peanut allergy	Overall food allergy	Source
Australia	Infants (12 months)	5276 ^b	9.00 (7.80–10.00)		3.00 (2.40–3.80)	10.40 (9.30–11.50)	[15, 16]
China	Infants (12 months)	477	2.50	1.30	0.00	3.80 (2.50–5.90)	[18]
South Africa	12–36 months	512 ^c	1.80 (0.60–2.90)	0.20 (0.00–0.60)	1.20 (0.20–2.10)	2.50 (1.40–4.30)	[17]
Norway	2.5 years (mean age)	2721	1.60 (1.30–2.00)				[52]
Turkey	1–24 months	614	1.30	0.16			[53]
Denmark	18 months	562	2.4	1.0		3.60	[54]
<i>EuroPrevall birth cohorts</i>							
Germany	Under 2 years of age	1440	2.01 (1.04–3.50)	0.47			[12•, 13•]
Greece	Under 2 years of age	844	0.07 (0.00–0.37)	0.00			[12•, 13•]
Iceland	Under 2 years of age	1292	1.29 (0.78–2.01)	0.54	0.15	1.86	[12•, 13•, 55]
Italy	Under 2 years of age	1007	1.58 (0.68–2.22)	0.29			[12•, 13•]
Lithuania	Under 2 years of age	1296	0.92 (0.11–3.32)	1.29			[12•, 13•]
Netherlands	Under 2 years of age	931	1.55 (0.83–2.63)	0.67			[12•, 13•]
Poland	Under 2 years of age	1343	0.95 (0.41–1.87)	0.71			[12•, 13•]
Spain	Under 2 years of age	1155	1.25 (0.57–2.36)	0.80			[12•, 13•]
United Kingdom	Under 2 years of age	872	2.18 (1.27–3.47)	0.56	0.60 (0.10–1.10)	2.10 (1.30–3.30)	[12•, 13•, 56, 57]

^a 95 % confidence intervals are included where these were provided in the source articles

^b Prevalence data were initially published as an interim analysis of the first 2848 study participants

^c Interim analysis

What Factors Might Explain the Migration Effect?

The increased risk of allergy among Australian-born infants of Asian migrant parents was seen across the spectrum of food allergies, and also for the related condition of eczema. This suggests that it is unlikely to be purely driven by differences in exposure to individual food allergens such as peanut in Asia compared with Australia. The fact that infants born in Australia to Asian migrant parents have a risk of food allergy that far exceeds the risk for Australian-born infants of non-Asian parents strongly supports a combined role of both genetics (or epigenetics) and the environment. Genetic polymorphisms more prevalent in the Asian population because of selective pressures of the Asian environment might increase the risk

of allergy when these environmental factors are removed following migration, or when new exposures occur to risk factors present in the Australian environment but not in the Asian environment. This also has important implications for the population living in Asia, as rapid “westernisation” of several Asian regions could therefore act in a similar way to lead to a rapid increase in food allergy in infants born into these environments.

A number of potentially interrelated environmental factors could be implicated, including humidity (with an impact on skin barrier function), microbial exposure (hygiene hypothesis), dietary changes (overall dietary patterns or age at first infant exposure to allergenic foods, or changes in dietary composition with respect to fibre, macro/micronutrient, or bio-active microbiological

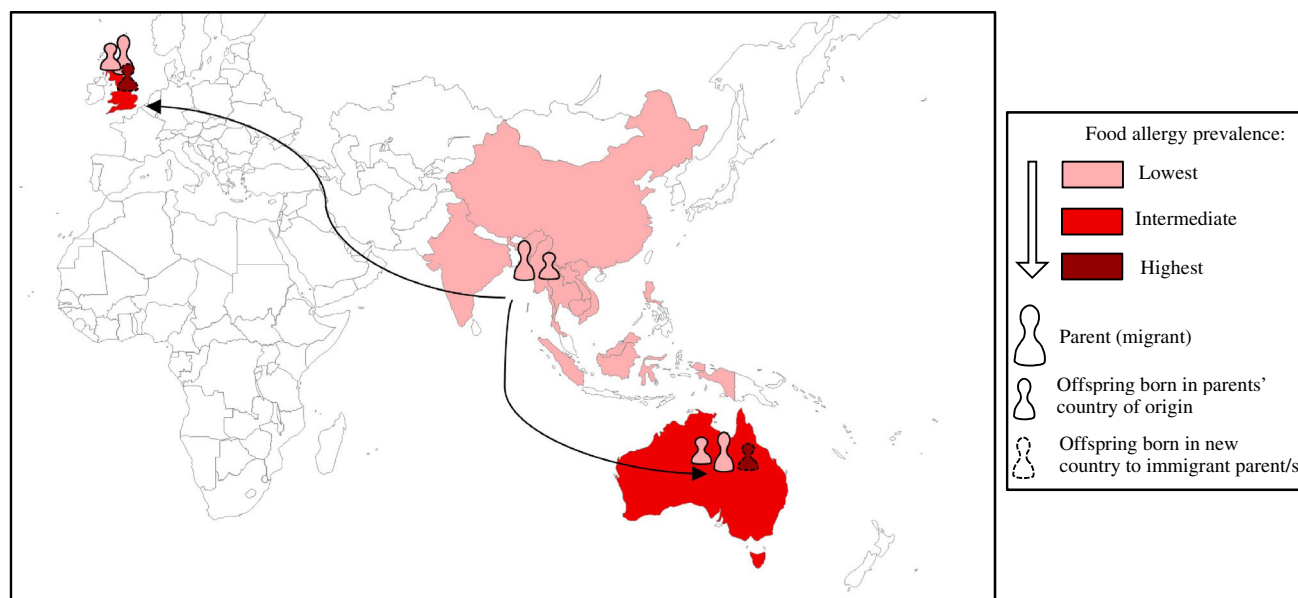


Fig. 2 Proposed effect of migration on food allergy risk across two generations. Individuals who migrate from Asia (a lower food allergy prevalence region) to Australia or the UK (higher food allergy prevalence regions) retain the lower risk of their country of origin (for

at least the first few years after migration). Children born to these immigrant parent/s have a risk of food allergy that exceeds that of not only their parents' country of origin, but also of the country into which they are born (Color figure online)

products such as short chain fatty acids) and changes in latitude (vitamin D) [28]. These factors could act directly through infant exposure (or lack of exposure) in utero or in the early postnatal period. Transgenerational effects may also be contributing, perhaps acting through epigenetic modifications. This could occur if maternal environmental exposures in the Asian country of origin affect the epigenetic signature of the offspring, such that the child growing up in a more Westernised country and lacking these same exposures, is at increased risk. Further investigation of this phenomenon has the potential to provide insights into the pathogenesis of food allergy.

Latitude Gradients in Food Allergy Prevalence—Can Greater Exposure to Vitamin D Decrease Food Allergy Risk?

Studies of different regions within the same country have consistently found that areas closer to the equator have less food allergy and/or fewer prescriptions of adrenaline auto-injectors and hydrolysed formulas used for treating cow's milk allergy [29–33]. The leading hypothesis to explain these findings is that greater year-round UV levels in these areas result in higher vitamin D exposure, with a subsequent protective effect against food allergy. Multiple mechanistic studies have shown a role for vitamin D in immune function and it has been hypothesised that adequate vitamin D exposure during development (either in

utero or in infancy) may be protective for food allergy [34]. However, studies of the association between maternal or birth vitamin D levels and offspring food allergy risk have shown conflicting findings [35, 36], while two studies in infants have shown an association between lower vitamin D levels and an increased risk of food allergy [36, 37]. Given the limitations inherent to observational studies of vitamin D levels in allergic disease risk, intervention trials are now ongoing to determine whether vitamin D supplementation in infancy can reduce the risk of children subsequently developing food allergy [38].

The Relationship Between Eczema and Food Allergy

A history of eczema is one of the strongest known risk factors for food allergy. A recent publication from the HealthNuts study showed that infants with eczema were approximately five times more likely to develop food allergy than infants without eczema. One in five infants with eczema had challenge-confirmed allergy to egg white, peanut or sesame by 12 months of age, compared to only one in 25 infants without eczema. The risk of food allergy increased with earlier age at onset and increasing severity of eczema, with approximately 50 % of infants whose eczema started in the first 3 months of life and required treatment with topical corticosteroids developing a food allergy [39•].

The association between eczema and food allergy could reflect shared genetic or environmental risk factors that increase the risk of both conditions, and/or a causal association whereby eczema itself increases the risk of food allergy. Several studies have consistently shown that filaggrin gene null mutations, which reduce an individual's ability to maintain an intact skin barrier, increase the risk of both eczema and food sensitisation [40, 41]. It has been hypothesised that a damaged skin barrier and the inflammation of the skin associated with eczema in infants could lead to penetration of the skin by food allergens, leading to an inappropriate immune response to these allergens [42].

The “Dual Allergen Exposure Hypothesis”, and Recent Advances in Preventing Peanut Allergy

While a less protective skin barrier may increase the risk of children developing food allergy, recent reports suggest that this could be overcome if the food is first introduced via the oral route. The “dual allergen exposure hypothesis” postulates that exposure to food allergens through the skin could result in food allergy if this is the first time an infant has been exposed to the food allergen. Conversely, if the first exposure to the food allergen occurs through the oral route, the infant is protected against the development of food allergy even with subsequent exposure through the skin [42]. This hypothesis is supported by mechanistic studies in animal models of food allergy, some observational epidemiological studies and more recently by the findings of an intervention trial, with most evidence focussed on peanut allergy. In animal models, exposure to peanut allergen through skin that has been damaged leads to food sensitisation and allergy [43]. This response was less pronounced in mice that had already developed tolerance by prior feeding of the allergen by the oral route. In observational studies, it has been shown that household consumption of peanut results in detectable levels of peanut allergen in the environment, and that increased household peanut consumption increases the risk of peanut allergy in infants who have not had any prior oral exposure to peanut [44]. This effect appears more pronounced in infants with a filaggrin gene mutation [45].

The dual allergen exposure hypothesis would suggest that food allergy is less common in regions with less eczema, earlier allergen exposure (so that first exposure to allergens occurs through the oral route) or both. Consistent with this, Du Toit, Lack and colleagues showed that Jewish children in Israel had very little peanut allergy compared with Jewish children in the UK, and that most infants in Israel started eating peanut in the first year of life, while most infants in the UK avoided peanut until after 1 year of age [46]. To test the hypothesis that earlier introduction of

peanut can prevent peanut allergy in high-risk children, the group then mounted an intervention trial where children with severe eczema and/or egg allergy were randomly assigned to either start eating peanut from 4 to 11 months of age or completely avoid peanut until 5 years of age [47•]. Infants were first screened for possible peanut allergy by skin prick testing, and 11 % of screened infants were excluded from the study because they were already likely to be peanut allergic at age 4–11 months (skin prick test wheal size >4 mm). In the remaining group of 640 infants, those who had consumed peanut starting from 4 to 11 months of age had an 81 % relative reduction in peanut allergy compared to those who had avoided peanut. This study provided the first evidence from a randomised trial that delayed introduction of peanut into the diet of high-risk infants increases the risk of peanut allergy.

Results of trials for early introduction of other foods have been less positive. In an egg allergy trial, giving high doses of egg powder at 4–6 months of age to high-risk children (with eczema) appeared to be associated with some reduction in egg allergy risk compared with egg avoidance until 8 months of age; however the difference between groups did not reach statistical significance and 31 % of infants in the early introduction of egg group had a reaction when the egg powder was first given, suggesting that egg allergy was already present at this early age in a significant proportion of infants with eczema [48]. A large trial of multiple allergenic food introductions from 3 to 6 months of age, compared with standard introduction from 6 months of age, did not find a significant difference in food allergy risk between the two groups in the primary intention-to-treat analysis [49•]. There are a number of possible explanations for this finding, including low compliance with the intervention protocol, or the difference in age at introduction between the two groups might have been too small to greatly alter food allergy risk.

What Impact Might a Shift Towards Earlier Introduction of Allergenic Foods Have on the Population Prevalence of Food Allergy?

In countries where peanut allergy is relatively common, including the US, UK and Australia, peanut avoidance during infancy was recommended for around a 10-year period from 1998 to 2008 (with some variation between countries). At the time of this advice, giving peanut products to infants in the first year of life was uncommon [46, 50]. The removal of this advice from guidelines was followed in Australia by a shift towards earlier peanut introduction in the next few years [50]. Current guidelines written by consensus of multiple international allergy organisations now recommend peanut be

introduced in the first year of life for infants with egg allergy or severe eczema [51]. Since there is now strong evidence that delayed introduction of peanut increases the risk of peanut allergy in high-risk infants, it is feasible that delayed introduction of peanut in high-risk infants contributed to the high prevalence of peanut allergy in these countries, and that a shift towards earlier peanut introduction will lead to fewer cases of peanut allergy in future generations.

There are however a few caveats that are important to note. Despite the great success of the early peanut introduction trial, likely peanut allergy (defined as a skin-prick test wheal size >4 mm) was already present in 10.6 % of high-risk infants screened at 4–11 months of age. Early introduction of peanut is not a feasible intervention strategy for these infants, since they are highly likely to react on consumption of peanut. Additional strategies will therefore need to be developed to prevent or treat peanut allergy for these infants. It is also important to note that although early peanut introduction prevented peanut allergy in a substantial portion of infants, the infants in the trial already had other allergic diseases in the form of severe eczema and egg allergy, and may have also had or developed allergies to other foods including tree nuts. Investigating intervention strategies to target the prevention of overall allergic disease risk therefore remains an important area of investigation.

Conclusions

There has been considerable progress in understanding the global prevalence of and risk factors for food allergy in the past 3 years. In particular, there is now good evidence that delayed introduction of peanut increases the risk of developing peanut allergy, and guidelines now recommend introduction of peanut in the first year of life for infants with pre-existing risk factors for peanut allergy. A shift towards earlier introduction of peanut in these infants may reduce the risk of peanut allergy in future generations. Recent progress in measuring the prevalence of food allergy in different regions of the world means that we now have good baseline data to measure the extent to which this intervention and others currently under investigation alter the prevalence of food allergy.

Compliance with Ethics Guidelines

Disclosure Jennifer J Koplin and Yichao Wang declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

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