Supporting document 1
Risk Assessment – Proposal P274
Review of Minimum Age Labelling of Foods for Infants

Executive summary

The appropriate timing for the introduction of solid foods to infants, also termed complementary feeding, is considered to be an important aspect of meeting an infant’s nutritional requirements in the first year of life. Infants should be introduced to solid foods when breastfeeding (or formula) no longer provides sufficient nutrients and when developmental cues indicate a readiness to receive solid food. However, the ideal time period in terms of various long and short term health outcomes has been debated over the past few years.

A number of international expert bodies including the World Health Organization (WHO), the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), and the European Food Safety Authority (EFSA) have reported views on timing of complementary feeding. The National Health and Medical Council (NHMRC) and New Zealand Ministry of Health (NZ MOH) have also issued recommendations stating that introduction of solid foods should occur when an infant is around 6 months of age. This recommendation differs from the current Standard 2.9.2 – Foods for Infants which refers to ‘4 months’ as the minimum age for labelling infant foods.

Therefore, the main purpose of this assessment is to determine whether any food-related safety risks would be linked to introduction of foods at ‘around 6 months’ compared to ‘from 4 months’.

Long- and short-term health outcomes that have been examined in relation to the timing of complementary feeding include nutritional adequacy (including energy intake), growth and overweight, developmental effects (including food preferences), renal function, infectious morbidity, and allergic diseases or syndromes. Because of the many differences and variables in study designs, it is difficult to link the specific timing (i.e. defined in months of age) to a health outcome. The strength of evidence for many of these associations is inconclusive due to studies where interpretation is complicated by study objectives which are separate to complementary feeding, such as duration of breastfeeding.

Because of the increase in the numbers of children observed with food allergy, sensitisation and anaphylaxis seen over the past 10-15 years, the association between allergic diseases and the timing of solid food introduction is of much current interest. In 2008, FSANZ reviewed the risk of allergy and other immune-mediated diseases in relation to timing of introduction of solid foods and concluded that, although preliminary information suggests that a small window may exist between 4 and 7 months to minimise allergy risk, conclusive evidence is still lacking. In 2009, reports published by EFSA and ESPGHAN gave similar conclusions.
As part of the Proposal P274, this risk assessment was undertaken to review the evidence for the appropriate timing for solid food introduction, focusing on reports and data published since 2008.

The main objectives were to identify adverse health outcomes associated with timing of solid food introduction relevant to the proposed change for the labelling of infant foods as appropriate for infants ‘around 6 months’. Food allergy risks were reviewed in detail because of current concerns which are particularly relevant to the time periods covered in this proposal.

The main conclusions of this assessment are summarised as follows:

- Solid foods introduced at ‘around 6 months’ compared to ‘from 4 months’ effectively means that introduction of solid foods could be delayed by as much as up to 2 months. Based on several key review articles, there are no health effects that are clearly linked with adverse outcomes if solid food introduction is delayed to ‘around 6 months’ compared to ‘from 4 months’.

- Allergy risk appears to be associated with solid foods introduced to infants at less than 4 months based on several cohort studies. This association combined with evidence that risk of infectious morbidity is also increased with this time period supports the current ESPGHAN and EFSA recommendations that ‘from 4 months’ is the appropriate minimum age at which solid foods are introduced.

- Since 2008, there is increasing evidence that the timing of solid food introduction may be related to the development of food-related allergy. The critical period to minimise the risk of allergy development seems to be between the ages of 4 and 7 months. However, because of unclear and inconsistent definitions of age categories, measurement bias in many studies, and the contribution of various other factors in the development of allergic disease, the evidence is not conclusive. Currently, there are randomised controlled trials (RCTs) underway which aim to determine whether exposure to food allergens, and not avoidance, is critical during this period to minimise the risk of developing food-related allergy and to determine the optimal timing for introduction of solid foods.

Therefore, based on current recommendations and the analysis presented in this risk assessment, the timing of ‘around 6 months’ as the appropriate age for the introduction of solid foods for infants would have minimal effect on the risk of adverse health outcomes compared to ‘from 4 months’.
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1. Introduction

Proposal P274 – Review of Minimum Age Labelling of Foods for Infants concerns an amendment to Standard 2.9.2 – Foods for Infants setting the labelling requirements for solid foods intended for infants.

The revised Australian *Infant Feeding Guidelines*, launched by the NHMRC in February 2013, recommended that solid foods be introduced to infants at ‘around 6 months’ (NHMRC 2013a). This recommendation is unchanged from the previous guideline issued in 2003 (NHMRC 2003). Likewise, the New Zealand *Food and Nutrition Guidelines for Healthy Infants and Toddlers* also recommends introduction of solid foods at ‘around 6 months’ (New Zealand Ministry of Health 2008). The timing for the introduction of solid foods in both guidelines is centered on ensuring adequate nutrient intake to infants when breast milk (or infant formula) may no longer be sufficient.

1.1. Objective of the assessment

This assessment provides an update of risk assessment work completed in 2008 and published as part of the Preliminary Final Assessment Report (PFAR) associated with Proposal P274 (FSANZ 2008). In relation to the timing of solid food introduction to infants, this assessment aims to:

- summarise the key conclusions of the PFAR
- summarise reviews or reports of international expert panels which have considered timing of complementary feeding for infants
- review published scientific data (particularly since 2008) that underlies Australian and New Zealand national infant feeding guidelines with emphasis on the induction of food allergy and/or gluten intolerance.

1.2. Scope of the assessment

Infant as defined under Standard 2.9.2 means a person up to the age of 12 months. Infant feeding practices up to the age of 12 months include breastfeeding, formula-feeding and, at an appropriate age, solid foods. Proposal P274 is relevant to the labelling requirements of foods intended for infants at around 6 months of age and this assessment will be directed at health effects associated with this time period. The health benefits of breastfeeding (exclusive or mixed with formula-feeding) for infants up to 6 months of age are well recognised and will not be addressed. Similarly, the inadvisability of introducing solids before 4 months of age is well recognised and will not be addressed.

1.3. Risk assessment questions

In relation to health effects associated with solid food introduction, information published in PFAR (FSANZ 2008) and recent reviews (see Section 2.3) were used to provide background summary and to identify any specific health effects to be assessed.

The risk assessment question addressed in this assessment (Section 3) is:

*What conclusions can be drawn from the evidence on the association between the age of introduction of solid food and the development of food-related allergies and/or gluten intolerance in children?*
1.4. Definitions

The following definitions apply to this risk assessment:

**Atopy** A child with atopy produces IgE antibodies after exposure to common environmental allergens. The atopic diseases (eczema, asthma and rhinoconjunctivitis) are clinical syndromes each defined by a group of symptoms and signs (Gold and Kemp 2005).

**Complementary feeding** is defined as the gradual introduction of solid food and fluids along with the usual milk feed (breast milk or infant formula) to an infant’s diet (New Zealand Ministry of Health 2008).

**Exclusive breastfeeding** refers to the WHO recommended definition which is breastfeeding with no additional liquid or solid foods other than vitamins and medications (Binns et al. 2009).

**Food allergy** (or food-related allergy) refers to food-mediated adverse reactions that involve the immune system resulting from oral exposure to food (Hayder et al. 2011).

**Food sensitisation** is an immune response to food allergen exposure which precedes development of food allergy

2. Background to this risk assessment

2.1. Previous FSANZ assessment

The previous FSANZ P274 nutrition assessment (FSANZ 2008) examined the following nutritional and developmental outcomes if introduction of solid foods were delayed to ‘around 6 months’:

- the potential for displacement of human breast milk and/or infant formula, any changes in energy intake, and whether growth outcomes are adversely affected
- the capacity of infant kidneys to deal with the higher solute load of solid foods prior to 6 months of age
- the impact on iron and zinc status, particularly in pre-term infants
- the influence of feeding practices during infancy on later food preferences.

The assessment concluded that in terms of infant growth, kidney function, and iron/zinc status, there is unlikely to be differences in the nutritional and developmental outcomes for infants that receive solids at an early (close to 4 months) versus a late (close to 6 months) age.

In addition, the relationship between age of introduction of solid foods and the development of allergies was assessed. Conclusions in this assessment, however, were more uncertain with some evidence suggesting that the delay in the introduction of solid food to infants’ diet may contribute to the risk of developing allergy and other immune-mediated diseases. FSANZ noted that this was an active area of research that was likely to increase the confidence around the optimal age for complementary feeding.

2.2. Recommendations of expert panels and committees

Recommendations on the appropriate age for the introduction of solid foods to infants have been issued by the World Health Organization (WHO) and several international scientific
panels including the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) and the European Food Safety Agency (EFSA). The views of these expert panels are based on consideration of several health outcomes and consensus on the benefits of breastfeeding for the first 6 months. However, recommendations are somewhat inconsistent for starting complementary feeding where timing of solid food introduction varies from 4 months compared to ‘around’ or ‘at’ 6 months of age (Table 1). These are subtle differences but may be important for certain health outcomes (addressed in Section 2.3).

Table 1: Comparison of recommendations for age of complementary feeding from Expert Panels and Committees

<table>
<thead>
<tr>
<th>Expert Body</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO (2003)¹</td>
<td>Recommends infants start receiving complementary foods at 6 months of age in addition to breast milk</td>
</tr>
<tr>
<td>ESPGHAN (2009)</td>
<td>Complementary feeding should not be introduced in any infant before 17 weeks and all infants should start complementary feeding by 26 weeks.</td>
</tr>
<tr>
<td>EFSA (2009)</td>
<td>Complementary food introduced between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects.</td>
</tr>
<tr>
<td>NZ MOH (2008)</td>
<td>Recommends that infants be fed exclusively on breast milk to around six months of age, at which time complementary foods can be introduced with continued breastfeeding.</td>
</tr>
<tr>
<td>NHMRC (2013)</td>
<td>Recommends introduction of solid foods at around 6 months of age.</td>
</tr>
</tbody>
</table>

The NHMRC recommendation is based on systematic reviews conducted as part of the review for the Australian Dietary Guidelines (NHMRC 2011). The findings of the systematic reviews were used to inform the Infant Feeding Guidelines which were published at the same time.

The initial literature search for the Australian Dietary Guidelines revealed evidence on the relationships between age of introduction of solid foods and development of overweight and development of allergic symptoms.

Subsequent systematic reviews on these two relationships indicated that:

(1) Overweight or obesity in children younger than 7 years of age, based on limited information (1 systematic review and 2 cohort studies; Grade D evidence) showed “no relationship between the age of weaning and development of infant or child overweight”.

¹ The WHO defines complementary feeding as foods or liquids that are provided along with breast milk and thus, infant formula is categorised as a complementary food. The intention of the WHO definition is to encourage exclusive breastfeeding until 6 months, particularly in developing countries where risk of infection from unsanitary food and water is significant (WHO 2003). In contrast, ESPGHAN and EFSA and others define complementary foods as all solid food and liquid foods other than breast milk or infant formula and follow-on formula. This assessment for P274 follows the ESPGHAN/EFSA definition.

² According to Appendix E of the Australian Dietary Guidelines, Grade D indicates that the evidence was limited, inconclusive, or contradictory. These Grade D relationships were not used to inform the development of the Guidelines.
(2) Development of allergic disease, based on limited information (1 systematic review, 2 RCTs, and 4 cohort studies; Grade D evidence), may be associated with the risk of allergic disease with some evidence that delaying the introduction until after 6 months may increase the risk of certain allergies. Details on the NHMRC review covering allergic syndromes is summarised in Section 3.

The NHMRC Infant Feeding Guidelines recommend introduction of solid foods at around 6 months based the nutritional sufficiency of breast milk until 6 months of age, development of feeding behaviour to allow chewing and swallowing, and maturity of the digestive system.

2.3. Summary of health effects associated with the timing of the introduction of solid foods

ESPGHAN and EFSA published comprehensive reviews on timing of complementary feeding in relation to a number of potential health effects (Agostoni et al. 2008; EFSA Panel on Dietetic Products Nutrition and Allergies (NDA) 2009). In addition, Hornell et al recently published a systematic review on infant feeding practices and covering similar health effects (Hornell et al. 2013). Attachment 1 lists the key findings from each review. Specific health outcomes examined included nutrient adequacy (including energy), growth (including obesity and overweight), allergic diseases, and infectious morbidity. The combined findings of these reviews indicate that:

- Deficiency of iron or zinc is unlikely if solid foods are introduced in the period of 4-6 months. However, data are lacking for nutrient intake if solids are introduced after 6 months.

- Age at which solid food is introduced does not have a strong impact on growth rates (weight or length) but data are lacking for solid foods introduced after 6 months. Interpretation of studies is complicated by differences in growth that result from changes in dietary composition (e.g. different complementary foods or increased milk protein).

- The evidence is insufficient to demonstrate that the timing of solid food introduction affects the risk of obesity or overweight.

- Solid food introduction before 6 months of age is a significant risk factor for infectious diseases in developing countries but in developed countries this association has only been observed when solid foods are introduced in infants less than 4 months of age.

- Increased risk of allergic syndromes (food allergy, atopy, gluten intolerance and/or celiac disease, and asthma) may be associated with the timing of complementary feeding, particularly if solid foods are introduced outside the 4–6 month period.

For the purposes of Proposal P274, analysis of studies on links between infant feeding practices and certain long- and short-term health outcomes is not straightforward. Studies frequently consist of double-barrelled questions and/or definitions so that health effects may be related to more than one issue. For example, studies focussed on determining the optimal duration of breastfeeding are important for understanding numerous infant health issues. However these same studies do not necessarily reveal the appropriate age for the introduction of solid foods. Very few studies have assessed the timing of complementary feeding as an independent risk factor. Specific factors contributing to definitional problems in studies examining the timing of solid food introduction include classification of formula as a complementary food, studies conducted solely on breastfed infants with no comparison with
formula-fed infants, and extrapolation of evidence from studies in developing countries to developed countries.

As an example of such definitional problems, the current WHO infant feeding guidelines are based in part on the ‘PROBIT’ observational cohort study which found lower gastrointestinal rates infection in infants exclusively breastfed for at least 6 months (Kramer et al. 2003). However, in relation to solid food introduction, the ‘PROBIT’ study only examined two populations: infants exclusively breastfed for 6 months and solid food introduced thereafter compared to infants exclusively breastfed for 3–4 months then solid foods and/or formula introduced. Therefore it is not possible to separate the effect of solids from the effect of formula on gastrointestinal infection incidence in the group with shorter breastfeeding duration. The incidence of gastrointestinal infection in infants who were introduced to solid foods at 3–4 months while continuing to be breastfed was not determined in this study. Furthermore, a recent large cohort study showed that the occurrence of gastrointestinal infection in infants requiring hospitalisation in their first year was linked to formula-feeding and not to solid foods (Quigley et al. 2009).

Apart from the potential links to allergic diseases, the three reviews covered in Attachment 1 indicate that there are no health effects clearly linked with adverse outcomes if solid food introduction is delayed to ‘around 6 months’ compared to from 4 months of age (see Attachment 1). The potential association to allergic diseases is consistent with conclusions of the FSANZ assessment conducted in 2008 (FSANZ 2008) and with recent published reviews (Palmer and Prescott 2012). Therefore, a more detailed analysis of this health effect will be addressed in Section 3.

3. Solid food introduction and allergy

Allergy is an abnormal immune response to a variety of exogenous proteins such as pollen, insect venom and food proteins. The development of allergic diseases is complex and depends on interactions between a variety of environmental factors and the genetic susceptibility of the individual. For food allergy, avoidance of potentially allergenic foods was originally considered to be important for susceptible individuals. Scientific evidence no longer supports this approach and oral tolerance (suppression of orally-induced immune responses in the gut) and timing of introduction and dose of potential food allergens are thought to be critical factors (Brandtzaeg 2010).

Common allergenic foods are cows’ milk protein, egg, soya, wheat, nuts and fish. Food allergy is an IgE-mediated immune response which is characterised by clinical outcomes or diagnoses such as atopic eczema (atopic dermatitis), allergic rhinitis and asthma. Food protein sensitisation precedes development of food allergy but does not always lead to an allergic disease for a given food.

For example, eczema is also a clinical symptom of food sensitisation, usually appearing in the first 18 months of age, which infants may outgrow in later childhood. Allergies to proteins in milk and egg increase risk of sensitization to pollen and development of asthma so that these health outcomes are also considered as food related.

The relationship between allergic disease and infant feeding has been covered in several recent reviews papers (Prescott et al. 2008; Prescott and Nowak-Wegrzyn 2011; Lack and Penagos 2011; Fewtrell et al. 2011; Palmer and Prescott 2012). The prevalence of allergic diseases and syndromes in children has increased substantially in the past 10–15 years.

Food-related allergy includes gluten intolerance which is an immune-mediated response to proteins in gluten and can give rise to celiac disease and Type 1 Diabetes Mellitus (FSANZ 2008).
The cause of this increase is not known but exposure to food proteins is considered to be an underlying risk factor with the type of food protein, exposure through the maternal diet, and the timing of exposure to specific food proteins under investigation. In addition, infants exposed to food proteins too early may develop allergic disease due to inefficient digestion of food proteins, undeveloped gut permeability, and degree of gut bacterial colonization (Shreffler and Radano 2011).

3.1. NHMRC review on age of introduction of solid foods and allergies

The relationship between development of allergies and appropriate timing for the introduction of solid foods was addressed within both the NHMRC Infant Feeding Guidelines (NHMRC 2013a) and the Australian Dietary Guidelines (NHMRC 2013b). The underlying scientific data supporting these guidelines was described in the Literature Review (NHMRC 2012) for the Infant Feeding Guidelines and the Evidence Report (NHMRC 2011) for the Dietary Guidelines.

The Literature Review for the Infant Feeding Guidelines considered the relationship of breastfeeding and formula-feeding to the prevention of atopic diseases and not timing of solid food introduction. However, the views and recommendations of various expert groups on the relationship between allergies and solid foods were also reviewed. Final comments suggested that there is no reason to restrict the introduction of any particular foods or groups of food to infants to prevent allergy or promote tolerance.

The Evidence Report for the Australian Dietary Guidelines was based on systematic reviews addressing specific targeted questions on food, diet and disease/health relationships including whether the age of solid food introduction in children is associated with the development of allergic syndromes (NHMRC 2011). The literature searches identified seven studies of which only four cohort studies and one RCT, all published between 2006 and 2008, were judged to be of suitable quality. Only two of the five studies examined introduction of solid foods in the 4–6 month time period and the other three involved introduction of solids after 6 months. The review concluded that the data suggests that delaying solid food introduction until after 6 months may increase the risk of certain allergies but acknowledged that the conclusion is based on a limited number of studies (Grade D evidence).

3.2. FSANZ analysis on the potential association between the age of solid food introduction and allergy

The analysis of review papers shown in Attachment 1 indicated that the age of introduction of solid foods is potentially associated with the development of allergic disease. This potential link was also identified in the FSANZ assessment conducted in 2008 (FSANZ 2008) and is consistent with recent published reviews (Palmer and Prescott 2012). Current concerns about food allergy risk are also particularly relevant to the time periods covered in Proposal P274. Therefore, a more detailed analysis of the evidence for this association is described below.
Sources of data, search strategy

Primary research (cohort study or RCT) was selected according to the PICO method and included the following study characteristics:

1. Breastfed or formula-fed infants of normal allergy risk or at-risk of allergic disease (parental history, allergic symptoms).
2. Various solid foods or specific allergenic foods (but not infant formula) introduced from 4 months of age.
3. Depending on the study, age of solid food introduction was compared to another specified age (e.g., introduction at 4 months compared to 6 months) or a non-allergenic food (e.g., egg compared to rice powder).
4. Outcomes were clinical diagnoses in infants and children up to age 10 years of food-related allergic diseases or symptoms: asthma, atopy or atopic disease, allergic rhinitis, allergic sensitization, celiac disease; Type 1 diabetes mellitus; eczema; food allergy, food sensitization, and wheezing.
5. Studies or specific analyses within studies that examined the duration of breastfeeding and association with allergic diseases were excluded.

The following strategy was used to source primary research:

1. Studies cited by reviews conducted by expert bodies (EFSA, ESPGHAN, the American Academy of Pediatrics (AAP), NHMRC). These mainly covered the period up to 2008 when these reports were completed or published.
4. Include only primary studies; position or consensus statements and review articles (apart from Palmer and Prescott, 2012) were excluded.

Studies identified through this approach are listed in Attachment 2. In summary, 27 studies covering the period of 1981–2013 were reviewed. Most were prospective cohort studies including infants of normal or increased allergy risk. The studies measured numerous allergic disease outcomes in infants and children spanning 1-10 years of age. The search of the PubMed database identified four additional studies published in 2013 not included in the other reviews (Palmer et al. 2013; Frederiksen et al. 2013; Nwaru et al. 2013a; Nwaru et al. 2013b).

One systematic review on the association of complementary feeding with the development of allergy was included in Attachment 2 (Tarini et al. 2006). The review’s conclusions are based on some of the primary research cited in this assessment plus several earlier publications. Allergy outcomes in relation to duration of breastfeeding also have been covered in several recent large systematic reviews (Kramer and Kakuma 2002; Kramer and Kakuma 2012) but, as mentioned in section 2.3, definitional issues mean that these reviews have limited use for proposal P274.

Results

Comparing studies is complicated by the variety of foods, timing of solid food introduction, allergy risk, different allergy outcomes, and age at assessment of outcome. To simplify analysis of these studies and address the question about the appropriate timing of solid food introduction, studies in Attachment 2 are grouped according to outcome:

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4 PICO defined as population (P), intervention (I), comparison (C) and outcome(s) (O).
Evidence that introduction before 4 months increases risk of allergic disease compared to introduction after 4 months. (1)

Evidence shows no association (protective or adverse) between the timing of solid food introduction and risk of allergic disease. (2)

Evidence that introduction of solid foods at around 6 months (i.e. after 4 months and before 7 months) is associated with decreased risk (or no increased risk) of allergic diseases compared to outside this age range. (3)

Introduction of solid foods before four months increased the risk of eczema in six cohort studies conducted from 1981 to 1994. These studies were mostly small cohort studies and most were also centred on the protective effects of exclusive breast feeding. These results are difficult to interpret because exclusive breastfeeding is often encouraged for at-risk infants (e.g. family history of allergic diseases) and so the results could reflect reverse causation (Zutavern et al. 2006). The evidence that allergy risk appears to be associated with solid foods introduced to infants at less than 4 months combined with evidence that risk of infectious morbidity is also increased with this time period continues to support the current recommendations from ESPGHAN, EFSA, AAP and NHMRC that 4 months of age is the appropriate minimum age at which solid foods are introduced.

Seven studies carried out from 1983 to 2011 showed neither protective nor adverse effects related to the age of solid food introduction and the risk of allergic disease. The lack of association was measured across various allergic diseases or symptoms and included one systematic review of 13 cohort studies (Tarini et al. 2006) showing association between the introduction of solids before the age of 3–4 months and development of eczema. However, little data were available to support an association between early introduction of solid food and other allergic conditions. A comparatively large cohort study (Chuang et al. 2011) showed that solid food introduction before 4 months, between 4–6 months, and after 6 months was not related to the risk of atopic disease in infants up to 18 months of age. Given the number of participants, this study provides strong support that the timing of solid food introduction across the period of ‘around 6 months’ does not influence the development of atopic diseases. The study recruited participants from the general population of newborns but excluded those infants with physician-diagnosed atopic dermatitis in the first 6 months of life to eliminate contribution of reverse causality. The inclusion of children with apparent normal allergy risk, however, may mean that immune-mediated food sensitisation, which underlies development of allergy, may not have occurred in these infants. These issues indicate the complexities in designing and interpreting studies on the development of allergies linked to dietary factors.

A number of studies (12 as listed in Attachment 2) published more recently (2006 to present) suggest growing evidence that exposure to allergenic foods between 4–6 months and/or before 7 months may decrease the risk of allergic diseases. As previously highlighted, mainly prospective, cohort studies have been conducted involving various time points, types of foods, and allergenic outcomes. These studies also support the view that avoidance of food allergens does not prevent allergic disease and that exposure to food in the period between 4 and 7 months may actually result in ‘tolerance’ rather than allergy.

3.3. Studies currently underway (RCTs)

Prescott and Palmer (2012) highlight the main issues with conclusions based on observational cohort studies conducted to date. Many studies on timing of complementary feeding do not account for ‘reverse causation’ which arises when an allergy outcome influences the exposure. For example, the children of allergic parents or infants showing early signs of allergy (eczema, for example) may be prescribed specific feeding practices (e.g. delayed solid food introduction) that are then interpreted as causative for increased risk of allergenic diseases measured at later time points (Zutavern 2006).
Most recent observational studies attempt to correct for reverse causation (e.g. Chuang et al, 2011) but numerous other factors are also not tested or controlled including timing of specific foods, quantity and quality of solid foods, influence of maternal exposure or environmental factors, and other routes of early allergen exposure that contribute to oral tolerance (Shreffler and Radano 2011; Lack and Penagos 2011). Several randomised controlled trials are now currently underway which will examine some of these factors and test the hypothesis that ‘early’ regular exposure to food allergens, induces oral tolerance and reduces the risk of allergic disease (Palmer and Prescott 2012; Metcalfe et al. 2013). Interventions involve introduction of various foods in the range of 3–8 months but with a clear focus on the 4–6 month period. Mostly results are yet to be published. In support of the early exposure hypothesis, recent results from a small RCT showed that the incidence of egg allergy at one year was reduced in sensitised infants fed egg protein from 4 months compared to infants on a normal diet with egg introduced at 8 months (Palmer et al. 2013).

3.4. **ASClA recommendation on timing of solid food introduction**

The Australasian Society for Clinical Immunology and Allergy (ASClA) issued a position statement on allergy and infant feeding based on systematic review of relevant papers and recommendations by other expert panels (ESPGHAN and AAP) (ASCIA 2010). Based on current evidence, ASCIA concluded that there is little evidence that delaying introduction of solid foods beyond 6 months reduces the risk of allergy and current expert reviews support the recommendation that solid foods should be introduced from around 4–6 months. The ASCIA statement also suggests that delays in solid food introduction beyond 6 months may actually increase the risk of allergy development but acknowledges that more research is needed to make conclusive recommendations about the timing of introduction of solid foods. ASCIA recommendations are based on primary studies and review articles as cited in this assessment.

3.5. **Summary**

Overall the evaluation of the studies listed in Attachment 2 suggests that the risk of allergic diseases or syndromes in children and infants to food is mainly linked to introduction of solids before 4 months and, possibly, after 7 months of age. Based on current evidence, the introduction of solid food at ‘around 6 months’ does not appear to present a greater risk of subsequent food allergy compared with introduction ‘from 4 months’. This conclusion is consistent with current advice and recommendations issued by several expert bodies. However, as concluded in the PFAR (2008), evidence continues to emerge that the period of 4–7 months may be the critical window for the prevention of food-related allergy. Most of the evidence is limited to observational cohort studies and current efforts are focussed on appropriate studies designed to address the specific questions of timing of complementary feeding in relation to allergy. These include several RCTs currently underway.

4. **Conclusions**

Response to risk assessment question

**What conclusions can be drawn from the evidence on the association between the age of introduction of solid food and the development of food-related allergies and/or gluten intolerance in children?**

Based on current national and international recommendations, and the analysis presented in this risk assessment, the timing of ‘around 6 months’ as the appropriate age for introduction of solid foods for infants would have minimal effect on the risk of adverse health outcomes compared to ‘from 4 months’.
Australian and New Zealand medical authorities (New Zealand Ministry of Health 2008; NHMRC 2013a) recommend introduction of solid foods to the infant diet at ‘around 6 months’ of age, largely based on assessment of the benefits of breastfeeding to this age.

A FSANZ review in 2008 found that there are unlikely to be differences in the nutritional and developmental outcomes for infants that receive solids at an early (close to four months) versus a late (close to six months) age. This is consistent with the current assessment where introduction of solids at ‘around 6 months’ compared to ‘from 4 months’ did not present any additional food safety risk to infants across a range of health outcomes including infectious morbidity, growth and micronutrient intake.

The evidence in relation to age of introduction of solids and subsequent development of allergic disease is uncertain but, based on current evidence, there does not appear to be any difference in risk of allergic disease when solids are introduced at any time within a critical window of 4–<7 months of age. There is some evidence that introduction before 4 months of age, and possibly after 7 months of age, is associated with increased allergy risk. Ongoing research in this area may help to clarify this relationship, when the research becomes available.
# Attachment 1: Health effects associated with age of complementary feeding

Table summarises the key findings and conclusion from three recent reviews on the timing of solid food introduction to infants and risk of adverse health outcomes. BF = breast feeding; EBF = exclusive breastfeeding; FF = formula-feeding; CF = complementary feeding

<table>
<thead>
<tr>
<th>Review Type</th>
<th>ESPGHAN¹</th>
<th>EFSA (2009)¹</th>
<th>HORNEILL ET AL (2013)²</th>
<th>CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main focus</td>
<td>Complementary feeding</td>
<td>Complementary feeding</td>
<td>Duration of exclusive breast feeding</td>
<td></td>
</tr>
<tr>
<td>Health effects:</td>
<td>Age of CF not specifically addressed.</td>
<td>Insufficient data – age of CF in terms of energy intake needs to be decided for individual infant (larger infants have greater energy requirements).</td>
<td>Association to duration of EBF examined: EBF to 6 months meets energy requirements and does not compromise infant growth.</td>
<td>Either no association or insufficient data to indicate the energy intake is compromised by age of introducing CF.</td>
</tr>
<tr>
<td>Energy intake</td>
<td>Timing of CF not specifically addressed although concluded that nutritional deficiencies during CF period (defined as after 17 weeks and before 26 weeks) are unlikely.</td>
<td>Reviewed studies on whether EBF provides adequate nutrients to 6 months; concludes that some infants need CF at 4–6 months for Fe and Zn sufficiency.</td>
<td>Not addressed.</td>
<td>No association but some infants may require solid foods at 4–6 months for Fe and Zn sufficiency.</td>
</tr>
<tr>
<td>Nutritional adequacy</td>
<td>CF introduced before 6 months does not have strong impact on growth rate. Late introduction (after 6 months) may reduce length and weight gain.</td>
<td>EBF for 4 months gives similar growth rates compared to EBF for 6 months.</td>
<td>No evidence of association between CF introduced at 4–6 months and growth rate.</td>
<td></td>
</tr>
<tr>
<td>Growth</td>
<td>No specific data on age of CF reviewed but limited evidence that low intake of LCPUFA (oily fish) and Fe may have adverse effect on neurodevelopment.</td>
<td>Insufficient data to make conclusion</td>
<td>Insufficient data to make conclusion</td>
<td></td>
</tr>
</tbody>
</table>

¹ ESPGHAN (2013) ² EFSA (2009)
<table>
<thead>
<tr>
<th>Food preferences</th>
<th>ESPGHAN¹</th>
<th>EFSA (2009)¹</th>
<th>HORNELL ET AL (2013)²</th>
<th>CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of CF not addressed but CF without added sugars and salt recommended.</td>
<td>Insufficient data to make conclusion</td>
<td>Not addressed.</td>
<td>Insufficient data to make conclusion</td>
<td></td>
</tr>
<tr>
<td>Renal function</td>
<td>Evidence indicates that renal function is sufficiently mature to metabolise nutrients from CF by the age of 4 months.</td>
<td>CF introduced after 4 months does not impact on renal function.</td>
<td>Not addressed.</td>
<td>CF introduced from 4 months is not associated with adverse renal function</td>
</tr>
<tr>
<td>Obesity, cardiovascular disease (CVD), and/or Type II diabetes (T2D)</td>
<td>Reviewed data on energy-dense complementary foods and protein intake in relation to obesity risk. No convincing evidence that age of CF is related to obesity risk or CVD.</td>
<td>Insufficient evidence to show that age of introduction of CF impacts on risk of obesity; no evidence that age of CF has effect on risk for T2D.</td>
<td>Any BF (including EBF) for longer than 4 months is protective against overweight and obesity in childhood.</td>
<td>Insufficient data to make conclusion on age of CF and risk of obesity, CVD, T2D. Some evidence that BF has protective effect.</td>
</tr>
<tr>
<td>Allergy, atopic disease, and/or asthma</td>
<td>Some evidence but limited that delayed introduction of CF beyond 4–6 months reduces allergies in infants (both normal and high risk infants)</td>
<td>Few studies examining the age of CF as independent risk factor for atopic diseases. No conclusion on appropriate age for CF.</td>
<td>Increased risk of eczema if CF introduced at &lt;4 months. Insufficient or limited evidence that risk of asthma and gluten intolerance are associated with timing of CF.</td>
<td>Yes, possible increased risk of allergy with introduction of solids outside the 4–6 month period.</td>
</tr>
<tr>
<td>Celiac disease (CD) and/or Type I diabetes mellitus (T1DM)</td>
<td>Introduction of gluten and other food allergens at 4–6 months (while breastfeeding) may have protective effects against CD and T1DM.</td>
<td>Progressive introduction of gluten between 4 and 6 months (while BF) may reduce risk of CD and T1DM.</td>
<td>Not addressed.</td>
<td>Yes, possible increased risk of allergy with delayed introduction of solids (i.e. later than 4–6 months)</td>
</tr>
<tr>
<td>Infectious morbidity: acute otitis media (AOM) and/or gastrointestinal</td>
<td>Age of CF not specially addressed. Infectious outcomes considered in terms of exclusive versus partial BF</td>
<td>Breastfeeding protects against infectious morbidity. Introduction of CF at 3 months or less may increase risk of infectious morbidity.</td>
<td>Any BF (including EBF) is protective against AOM</td>
<td>Insufficient evidence to make conclusion on association of CF and infectious disease. Evidence of association primarily based of protective effects of BF.</td>
</tr>
<tr>
<td>KEY FINDINGS: EVIDENCE THAT SOLID FOOD INTRODUCTION AT ‘AROUND 6 MONTHS’ MAY CONTRIBUTE TO ADVERSE HEALTH OUTCOMES</td>
<td></td>
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<td>---------------------------------------------------------------</td>
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</tr>
<tr>
<td><strong>ESPGHAN</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td><strong>EFSA (2009)</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td><strong>HORNELL ET AL (2013)</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td><strong>CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Dental health</strong></td>
<td>No conclusions on risk of caries and age of CF</td>
<td>No evidence that age of CF is related to having caries.</td>
<td>Not addressed.</td>
<td>Insufficient data to make conclusion</td>
</tr>
</tbody>
</table>

<sup>1</sup> Both ESPGHAN and EFSA define CF as the period when complementary foods are given together with either human milk or a breast milk substitute.

<sup>2</sup> Atopic disease, asthma and allergy were the only health outcomes that were examined specifically in relation to introduction of CF (other health outcomes examined were in relation to duration of breastfeeding, as noted).
### Attachment 2: Allergy and association with age of complementary feeding

Table summarises primary studies investigating the link between age of introduction of solid foods and risk of food-related allergy, allergic diseases and syndromes. Studies were selected as described in Section 3.2. Columns on far right indicate where study has been cited by major review publications. See References for citation details. BF = any breast feeding; EBF = exclusive breastfeeding; FF = formula-feeding; CF = complementary feeding.

<table>
<thead>
<tr>
<th>Study (location)</th>
<th>Type &amp; Population</th>
<th>N</th>
<th>Effect</th>
<th>Age assessed</th>
<th>Exposure variable (foods introduced; time period)</th>
<th>Outcome</th>
<th>Cited by</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Evidence shows early (before 4 mo) increases risk of allergic disease</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1981 Fergusson (New Zealand)</td>
<td>Cohort ± parental history of atopy</td>
<td>1265</td>
<td>E</td>
<td>2 yr</td>
<td>Solid foods at before/after 4 mo in breastfed and formula-fed infants</td>
<td>Solid foods introduced before 4 mo increases risk of E in both breastfed and formula-fed infants</td>
<td>✓</td>
</tr>
<tr>
<td>1983 Kajosaari (Finland)</td>
<td>Cohort w/ history of atopy</td>
<td>135</td>
<td>E, FA</td>
<td>1 yr</td>
<td>Solid foods introduced at 3 mo compared to 6 mo to EBF infants</td>
<td>Early solid food introduction (3 mo compared to 6 mo) increases risk of E, FA</td>
<td>✓</td>
</tr>
<tr>
<td>1990 Fergusson (New Zealand)</td>
<td>Cohort; Normal allergy risk</td>
<td>1265</td>
<td>E</td>
<td>0-10 yr</td>
<td>Various foods at before/after 4 mo</td>
<td>Solids introduced before 4 mo increases risk of E</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>1991 Kajosaari (Finland)</td>
<td>Cohort w/ history of atopy</td>
<td>135</td>
<td>AD, FA</td>
<td>5 yr</td>
<td>Solid foods introduced at 3 mo compared to 6 mo to EBF infants</td>
<td>At 1 yr, delayed solid foods to 6 mo (compared to 3 mo) reduces risk of E, FA but no difference at 5 yr.</td>
<td>✓</td>
</tr>
<tr>
<td>1994 Kajosaari (Finland)</td>
<td>Cohort w/ history of atopy</td>
<td>135</td>
<td>E, FA</td>
<td>1 yr</td>
<td>Solid foods introduced at 3 mo compared to 6 mo to EBF infants</td>
<td>Delayed solid foods to 6 mo (compared to 3 mo) reduces risk of E, FA</td>
<td>✓</td>
</tr>
<tr>
<td>2004 Morgan (UK)</td>
<td>Cohort; pre-term infants</td>
<td>257</td>
<td>E</td>
<td>1 yr</td>
<td>Solid foods before 17 weeks compared to after 17 weeks in EBF, BF, and FF infants</td>
<td>Introduction of 4 or more solid foods before 17 weeks increased risk of E</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Evidence shows no association (protective or adverse effects) between age of introduction and risk of allergic disease</strong></td>
<td></td>
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</tr>
<tr>
<td>1983 Fergusson (New Zealand)</td>
<td>Cohort; Normal allergy risk</td>
<td>1110</td>
<td>A, W</td>
<td>0-4 yr</td>
<td>Solid foods before 4 mo compared to after 4 mo in EBF and BF infants</td>
<td>No association between solids introduced before 4 mo and risk of A; BF in first 4 mo does not reduce incidence of A.</td>
<td>✓</td>
</tr>
<tr>
<td>2002</td>
<td>Cohort; w/</td>
<td>1321</td>
<td>AD</td>
<td>1 yr</td>
<td>Egg/milk introduced before 4 mo</td>
<td>Age of introduction of solid foods was not</td>
<td>✓</td>
</tr>
<tr>
<td>Study (location)</td>
<td>Type &amp; Population</td>
<td>N</td>
<td>Effect</td>
<td>Age assessed</td>
<td>Exposure variable (foods introduced; time period)</td>
<td>Outcome</td>
<td>Cited by</td>
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</tr>
<tr>
<td>Schoetzau</td>
<td>history of atopy</td>
<td></td>
<td></td>
<td></td>
<td>compared to after 4 mo</td>
<td>associated with incidence of AD</td>
<td>ES A N</td>
</tr>
<tr>
<td>2004 Zutavern (UK)</td>
<td>Cohort; Normal allergy risk</td>
<td>605</td>
<td>W, A, E</td>
<td>5.5 yr</td>
<td>Various foods at time points between 3 and 9 mo</td>
<td>No evidence that later introduction protects against W, A, E. Increased risk of E with eggs at &gt; 8 mo.</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>2006 Zutavern (UK)</td>
<td>Cohort + allergic symptoms</td>
<td>2612</td>
<td>AD, AS</td>
<td>2 yr</td>
<td>Egg and milk introduced before 6 mo compared to after 6 mo</td>
<td>No evidence that introduction of solids after 6 mo reduces risk of AD, AS</td>
<td>✓ ✓</td>
</tr>
<tr>
<td>2009 Kramer (Belarus)</td>
<td>Cohort</td>
<td>2951</td>
<td>AD</td>
<td>6.5 yr</td>
<td>EBF for 6 mo compared to EBF for 3 mo then introduce solids or milk</td>
<td>No association between EBF duration or age of solid food introduction and A</td>
<td>✓</td>
</tr>
<tr>
<td>2011 Chuang (Taiwan)</td>
<td>Cohort; Normal allergy risk</td>
<td>1877</td>
<td>AD</td>
<td>18 mo</td>
<td>Solid foods before 4 mo, between 4–6 mo, and after 6 mo.</td>
<td>No association between age of introduction and risk of AD</td>
<td>✓</td>
</tr>
<tr>
<td>2006 Tarini</td>
<td>Systematic review</td>
<td>N/A</td>
<td>E, AS, W, FA, AR, AD</td>
<td>1-10 yr</td>
<td>13 cohort studies; some with family history of allergy</td>
<td>Evidence for risk of allergy with solids at &lt; 4 mo is inconsistent (possible increased risk for E with solids at &lt; 4 mo)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td><strong>Evidence that introduction of solid foods at around 6 months (i.e. after 4 mo and before 7 mo) is associated with decreased risk (or no increased risk) of allergic diseases</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2006 Poole (USA)</td>
<td>Cohort; Normal allergy risk</td>
<td>1612</td>
<td>FA (wheat)</td>
<td>1-4yr</td>
<td>Wheat introduced before 6 mo compared to after 6 mo</td>
<td>Cereal grain/rice introduced after 6 mo increased risk of wheat allergy</td>
<td>✓</td>
</tr>
<tr>
<td>2008 Snijders (Netherlands)</td>
<td>Cohort; Normal allergy risk</td>
<td>2558</td>
<td>AD, AS</td>
<td>2 yr</td>
<td>Solid foods introduced before 7 mo compared to after 7 mo</td>
<td>Solids introduced after 7 mo increases risk for E, AD, AS, but not FS</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>2007 Filipiak (Germany)</td>
<td>Cohort, ± allergy risk</td>
<td>4753</td>
<td>E</td>
<td>4 yr</td>
<td>Various foods introduced before 4 mo, during 5-6 mo and after 7 mo</td>
<td>Delayed introduction of solids after 4 months or, for highly allergenic foods (e.g. nuts) after 6 months of age decreases risk of E compared to introduction after 7 months.</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>2008 Zutavern (UK)</td>
<td>Cohort; ± allergic symptoms</td>
<td>2073</td>
<td>A, AR, AS</td>
<td>6 yr</td>
<td>Solid foods before 4 mo, from 4–6 mo, and after 6 mo. (“late introduction” means after 4 or 6 mo)</td>
<td>Solids foods introduced after 4 mo increases risk of FS, E. No association between solid foods introduced at 4–6 months and risk of A, AR.</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>2010 Koplin (Australia)</td>
<td>Cohort; Normal allergy</td>
<td>2589</td>
<td>FA</td>
<td>12 mo</td>
<td>Egg introduced 4–6 mo compared to after 6 mo</td>
<td>Introduction after 6 mo associated with increased risk of egg allergy</td>
<td>✓</td>
</tr>
<tr>
<td>Study (location)</td>
<td>Type &amp; Population</td>
<td>N</td>
<td>Effect¹</td>
<td>Age assessed</td>
<td>Exposure variable (foods introduced; time period)</td>
<td>Outcome</td>
<td>Cited by²</td>
</tr>
<tr>
<td>------------------</td>
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</tr>
<tr>
<td>2010 Hesselmar (Sweden)</td>
<td>Cohort; Normal allergy risk</td>
<td>184</td>
<td>A, E</td>
<td>18 mo</td>
<td>Fish introduced over various ages in first year</td>
<td>16% increased prevalence of E for every 2 mo delay in fish introduction</td>
<td>✓</td>
</tr>
<tr>
<td>2010 Nwaru. (Finland)</td>
<td>Cohort; ± diabetes risk</td>
<td>994</td>
<td>AS</td>
<td>5 yr</td>
<td>Various foods introduced from 4 to 10 months</td>
<td>Late introduction of potatoes (&gt;4 mo), oats (&gt;5 mo), rye (&gt;7 mo), wheat (&gt;6 mo), meat (&gt;5.5 mo), fish (&gt;8.2 mo), and eggs (&gt;10.5 months) increases risk allergic sensitisation.</td>
<td>✓</td>
</tr>
<tr>
<td>2010 Virtanen (Finland)</td>
<td>Cohort; Normal allergy risk</td>
<td>1293</td>
<td>A</td>
<td>5 yr</td>
<td>Various foods over first year; Oats introduced before and after 5.5 mo</td>
<td>Early introduction of oats (&lt;5.5 mo) decreases risk of A compared to introduction after 5.5 mo</td>
<td>✓</td>
</tr>
<tr>
<td>2013 Nwaru (Finland)</td>
<td>Cohort; ± atopic risk</td>
<td>3781</td>
<td>A, AD, E</td>
<td>2 yr &amp; 5 yr</td>
<td>Various foods from 3–7 mo.</td>
<td>Early introduction (time specific to each food) decreases risk of A, AD, E</td>
<td>✓</td>
</tr>
<tr>
<td>2013 Nwaru (Finland)</td>
<td>Cohort; ± atopic risk</td>
<td>3781</td>
<td>AS</td>
<td>5 yr</td>
<td>Various foods at 3–11 mo to EBF, BF and FF infants.</td>
<td>Early introduction (time specific to each food) decreases risk of AS</td>
<td>✓</td>
</tr>
<tr>
<td>2013 Frederiksen (USA)</td>
<td>Cohort; at-risk for T1DM</td>
<td>1835</td>
<td>D</td>
<td>From 9 months</td>
<td>Various foods introduced at &lt;4 months and ≥6 months</td>
<td>Risk of T1DM was increased at early (&lt;4 months) or late (≥6 months) exposure times compared to 4-5 months</td>
<td>✓</td>
</tr>
<tr>
<td>2013 Palmer (Australia)</td>
<td>RCT; with mild-severe eczema</td>
<td>86</td>
<td>FA</td>
<td>8 &amp; 12 mo</td>
<td>Daily egg powder compared to rice powder fed between 4–8 months</td>
<td>Incidence of egg allergy lower with egg exposure from 4 months compared to 8 months.</td>
<td>✓</td>
</tr>
</tbody>
</table>

Evidence or age range for solid food introduction not applicable to P274 assessment

<table>
<thead>
<tr>
<th>Study (location)</th>
<th>Type &amp; Population</th>
<th>N</th>
<th>Effect¹</th>
<th>Age assessed</th>
<th>Exposure variable (foods introduced; time period)</th>
<th>Outcome</th>
<th>Cited by²</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006 Kull (Sweden)</td>
<td>Cohort; Normal allergy risk</td>
<td>2614</td>
<td>A, AR, AS, E</td>
<td>4 yr</td>
<td>Fish at before 9 months (3–8 months) compared to 9 mo</td>
<td>3-8 mo group had reduced risk for A, E, AR, AS</td>
<td>✓</td>
</tr>
<tr>
<td>2009 Alm (Sweden)</td>
<td>Cohort; Normal allergy risk</td>
<td>4953</td>
<td>E, FA</td>
<td>12 mo</td>
<td>Fish introduced before 9 mo compared to after 9 mo</td>
<td>Early introduction decreases risk of eczema</td>
<td>✓</td>
</tr>
<tr>
<td>2011 Joseph (USA)</td>
<td>Cohort; ± allergy risk</td>
<td>594</td>
<td>AD, AS</td>
<td>2 yr</td>
<td>Solid foods before 4 mo compared to after 4 mo</td>
<td>For infants with parental history of allergy, peanut sensitisation and possibly egg was reduced in infants exposed at &lt;4mo</td>
<td>✓</td>
</tr>
</tbody>
</table>

¹Effect abbreviations: A = asthma; AD = atopic disease; AR = allergic rhinitis; AS = allergic sensitization; At = atopy; C = celiac disease; T1DM = type 1 Diabetes Mellitus; E = eczema; FA = food allergy; FS = food sensitization; W = wheezing

References


NHMRC (2011) A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines. National Health and Medical Research Council, Canberra


