TIMING OF INTRODUCTION OF ALLERGENIC FOODS IN INFANTS, AND RISK OF FOOD ALLERGY (FA)

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1. Timing of introduction of allergenic foods and risk of Food Allergy (FA) – summary of interventions and findings

Key information about each study is shown in the Table of Study Characteristics (Table 1), and summarised below.

1.1. Studies identified

We identified 15 intervention studies which reported the association between timing of introduction of allergenic food(s) and risk of FA. Of these, 12 were randomised control trials, 2 quasi-randomised trials and 1 controlled clinical trials. Three studies used a multifaceted intervention.

1.2. Populations

The majority of studies (n=8) were carried out in European populations, other studies were undertaken in North America (n=2) and Asia-Pacific region (n=5). Overall over 5000participants were allocated to intervention arms, and over 5000participants to control arms.

1.3. Interventions and comparators

Current UK Government advice is for the introduction of allergenic food into the infant diet to be delayed until 6 months of age or later. In this report we describe intervention studies of two types:

'Standard' intervention trials where comparisons have been made between giving no advice about introduction of allergenic foods (intervention), with advice to deliberately delay introduction of allergenic foods (control).

'Early' intervention trials in which comparisons have been made between deliberate early introduction of allergenic food(s) (intervention), with either no advice about introduction, or advice to delay introduction of allergenic foods (control).

For our purposes in both types of study the early or unrestricted introduction of allergenic foods is considered as being the 'intervention', and the delayed or standard introduction of allergenic foods as being the 'control'. The reason for this is so that, where appropriate, both types of study can be incorporated into the same meta-analysis.

Cow's milk was used in the intervention group in 9 studies (as early intervention in 2 and standard in 7); egg in 9 studies (early intervention in 5 and standard in 4); fish in 4 studies (early intervention in 1 and standard in 3); soya in 3 studies all as standard; peanut in 3 studies (early intervention in 2 and standard in 1); wheat in 3 studies (early intervention in 1 and standard in 2); other nuts (tree nuts) in 2 studies all as standard; sesame in 1 study as early intervention.

1.4. Outcome assessment methods used

Food allergy was assessed using parental report of symptoms (n=1) and/or study doctor assessment (n=3), parent report of doctor diagnosed food allergy (n=3), or most commonly oral food challenge (n=9) (not mutually exclusive). Twelve studies assessed food allergy at age 0-4, six studies at ages 5-14 and one at age 15 and over. Four studies assessed food allergy at more than one timepoint.

1.5. Risk of bias assessment

Overall risk of bias was considered high in 6 studies (40%), due to a combination of attrition bias (n=2) and selection bias (n=4). Only 2 studies had low overall risk of bias. Two studies were considered at high risk of bias due to conflict of interest.

1.6. Key findings

i. We found MODERATE evidence (-1 indirectness) that introduction of egg at 4-6 months reduces risk of egg allergy, compared with later introduction of egg.

ii. We found MODERATE (-1 indirectness; -1 imprecision; +1 strong effect size) evidence that peanut introduction at 4-11 months reduces risk of peanut allergy, compared with later introduction.

iii. We found no evidence for a general relationship between timing of allergenic food introduction and FA to the same food across differing interventions and study populations.

Table 1 Characteristics of intervention trials evaluating timing of allergenic food introduction in infants and FA

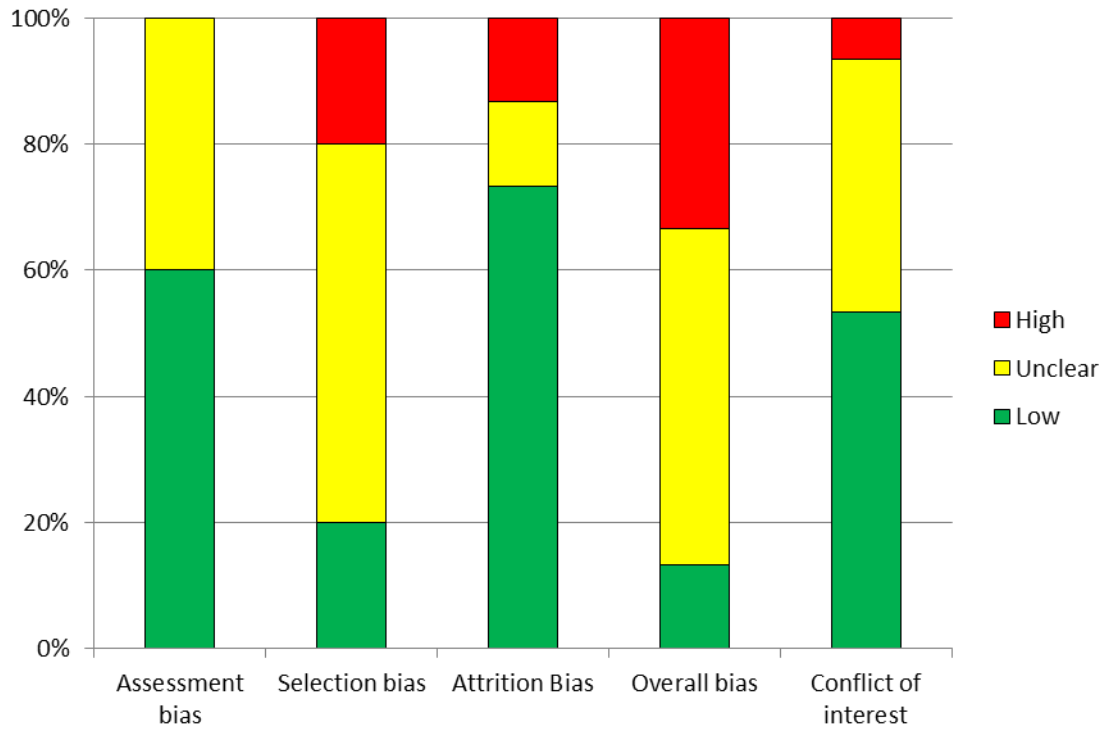
Study	Design	N Int/ Ctrl	Intervention	Population	Country	Disease risk	Age	Outcome assessment
Bellach, 2016 (1)	RCT	184/ 199	Pasteurised egg white powder versus rice powder 3 times per week from 4-6 months to 12 months	**HEAP Study.** Infants aged 4-6 months with specific IgE to egg <0.35 kU/L	Germany	Normal	1	Oral food challenge
Du Toit, 2015/16 (2, 3)	RCT	319/ 321	6g peanut protein per week, divided between 3 meals, from 4-11 months to 5 years, versus peanut avoidance.	**Learning Early About Peanut allergy (LEAP) Study**. Infants aged 4-11 months with severe eczema and/or egg allergy and peanut SPT <4mm. Mean 7.8 months.	UK	High	5, 6	Oral food challenge
Halmerbauer, 2002/3 (4, 5)	RCT	347/ 349	**MULTIFACETED**. Standard care versus e BF ≥ 3 months, delayed solid (≥6 months) and allergenic food (milk, egg, fish, nuts ≥1 year), and environmental control.	**Study on the Prevention of Allergy in Children in Europe (SPACE)**. ≥1 parent with a positive allergy history plus aeroallergen sensitisation.	UK, Germany, Austria	High	1	DD food allergy
Halpern, 1973 (6)	RCT	~875 / 875	Egg yolk given before 3 weeks, versus after 6 months.	Caucasian infants seen at birth by one of 11 private paediatricians in Dallas.	USA	Normal	5	Oral food challenge
Hide, 1994/6 (7, 8) Arshad, 1992/ 2003/7 (9-11) Scott, 2012 (12)	RCT	68/ 71	**MULTIFACETED**. Standard care versus cow's milk, egg, wheat, nuts, fish and soya excluded from diet of infant and lactating mother to 9 months, soya hydrolysate if needed, environmental control.	**Isle of Wight Study**. Infants with a first degree relative affected by an allergic disorder plus cord blood IgE>O.5kU/L.	UK	High	1, 8, 18	Parental report +/- oral food challenge

Study	Design	N Int/ Ctrl	Intervention	Population	Country	Disease risk	Age	Outcome assessment
Lowe, 2011 (13)	RCT	206/ 208	Cow's milk versus soya formula, as needed from birth. Introduced at median 4 months.	**Melbourne Atopy Cohort Study (MACS).** Infants with a first degree relative with eczema, asthma, AR or food allergy.	Australia	High	7	Physician assessment
Natsume, 2016 (14)	RCT	60/ 61	Heated egg powder (50mg daily from 6-9 months; 250mg daily from 9-12 months) versus placebo from 6 to 12 months	Infants with atopic dermatitis by 4-5 months.	Japan	High	1	Oral food challenge
Palmer, 2013 (15)	RCT	49/ 37	1 teaspoon per day of pasteurized raw whole egg powder, versus rice flour powder, given daily from randomization at 4 months to 8 months age.	Singleton term infants with symptoms of moderate-to-severe eczema.	Australia	High	1	Oral food challenge
Perkin, 2016 (16)	RCT	652/ 651	Sequential introduction of six allergenic foods - cow's milk, peanut, egg, wheat, sesame and fish from age 3 months (median 17 weeks milk, 21 weeks wheat, 20 weeks other allergens), versus avoidance to ≥6 months.	**Enquiring About Tolerance (EAT) Study.** Children exclusively breastfed at 3 months and gestation over 37 weeks.	UK	Normal	3	Oral food challenge
Tan, 2016 (17)	RCT	165/ 154	Pasteurised whole egg powder (350mg egg protein) daily versus rice powder from the time of solid food introduction (median 4 months) until 8 months age.	BEAT Study. Infants with a first degree relative with allergic disease, and egg SPT <2mm at age 4 months.	Australia	High	1	Oral food challenge

Study	Design	N Int/ Ctrl	Intervention	Population	Country	Disease risk	Age	Outcome assessment
Zeiger, 1989/92/94 (18-20)	RCT	~185 / 103	**MULTIFACETED**. Standard care versus infants cow's milk/ wheat/soy/egg/peanut/fish avoidance to ≥1 year & maternal allergenic food avoidance during pregnancy/ lactation.	Infants covered by Kaiser Permanente Health Plan, with an allergic parent.	USA	High	2, 4, 7	DD food allergy
Zhou, 2014 (21)	RCT	99/ 101	Cow's milk versus goat milk formula from <2 weeks age.	Healthy term infants fully formula fed within 2 weeks of birth.	Australia	Normal	1	Medically diagnosed food allergy - not otherwise defined
Juvonen, 1994 (22)	qRCT	~43/ 58	Cow's milk formula versus breast milk for first 3 days of life.	Healthy term infants.	Sweden	Normal	0.17	Physician assessment
Saarinen, 2000 (23)	qRCT	1789 / 1859	Cow's milk formula versus pasteurised human milk from birth for mean 4 days.	Term infants in Helsinki fed formula milk before hospital discharge.	Finland	normal	2	Oral food challenge (cow's milk)
Lindfors, 1988 (24) Lindfors, 1992 (25)	CCT	112/ 104	Cow's milk formula given as first meal and increased to ≤60 ml every 4 hours, until breastfeeding started; versus breastfed from birth.	Healthy low birth weight infants with gestational age 37-42 weeks.	Sweden	Normal	1.5, 5	Physician assessment

BF breastfeeding; eBF exclusive breastfeeding; RCT randomised clinical trial, qRCT quasi-randomised controlled trial, CCT controlled clinical trial; SPT skin prick test, BHR bronchial hyperresponsiveness, FEV_1 forced expiratory volume in one second; Physician assessment refers to assessment by a study physician , DD refers to community diagnosis

Figure 1 Risk of bias in intervention studies of timing of allergenic food introduction and risk of FA



2. Timing of cow's milk introduction and risk of FA

2.1. Short term early cow's milk introduction and FA

Figures 2 to 4 show data from studies of short term early cow's milk introduction (where the intervention period was limited to the first week of life, and did not extend beyond this) and risk of FA-CM (Figure 2) or FA-Any (Figures 3 and 4). Data are sparse, and there is no statistically significant association seen. The qRCT of Juvonen 1994 reported FA-CM at age 2 months, assessed as clinical features such as urticaria and intestinal symptoms following cow's milk exposure. The authors reported no cases of FA-CM in either the early cow's milk or human milk control group.

Figure 2 Short term early cow's milk introduction and risk of FA-CM at ≤4 years

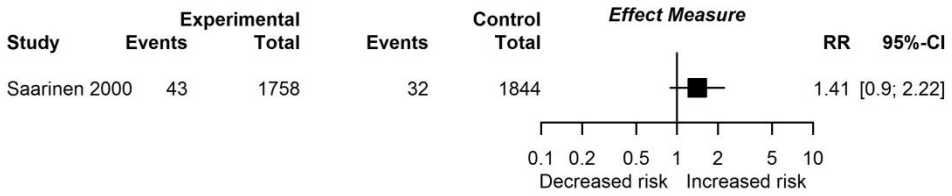


Figure 3 Short term early cow's milk introduction and risk of FA-Any at age ≤ 4 CCT

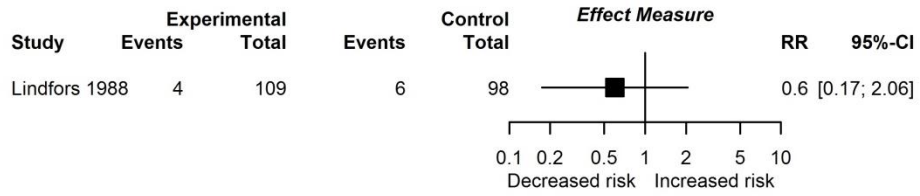
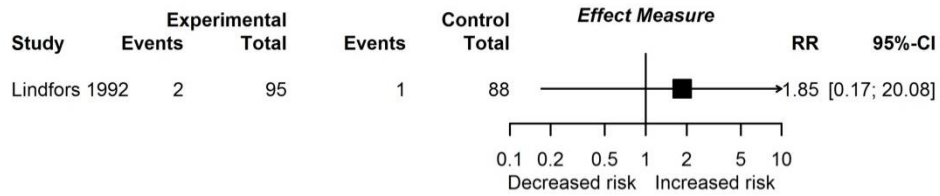


Figure 4 Short term early cow's milk introduction and risk of FA-Any at age 5-14 CCT



2.2. Studies of longer term early cow's milk introduction and FA

Figures 5 to 8 show data from studies of longer term early cow's milk introduction (where the intervention period was during infancy, but was not restricted to the first week of life) and risk of FA. We did not find evidence of an association with FA-Any, FA-CM or FA-Egg at age ≤4. Perkin 2016 also reported FA-Peanut, with no significant difference. Two multifaceted intervention trials found increased risk of FA-Any at age 5-14 in participants who had unrestricted use of cow's milk in infancy, compared with participants advised to delay introduction of cow's milk as part of a multifaceted intervention (Figure 6). This meta-analysis is also found in the sections on egg (Figure 15), nut (Figure 20), fish (Figure 27), wheat (Figure 32) and any allergenic food (Figure 34) due to the multifaceted nature of the intervention used. The meta-analysis is therefore not discussed in detail in these other sections, to avoid repetition.

One of the two studies contributing to this meta-analysis (Arshad 1992; Isle of Wight) separately reported no significant difference in doctor diagnosed food allergy by age 1 (Figure 4) or by age 2 – OR 1.25 (95% CI 0.27, 5.79). The other study (Zeiger (18)) separately reported food allergy in graphical form in 225 participants at age 4, which could not be included in meta-analysis. They found increased FA to any food in the standard advice group when using lifetime prevalence, but no significant difference when using 12-month prevalence at age 4.

Figure 5 Early cow's milk introduction and risk of FA-Any at age ≤ 4 years

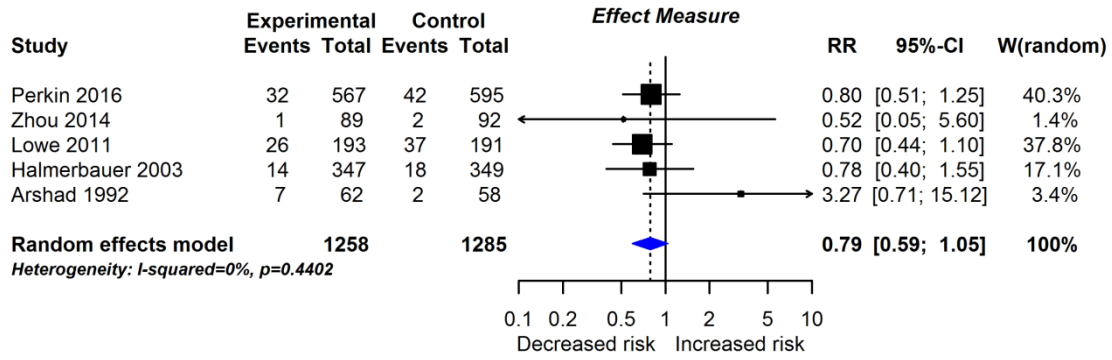
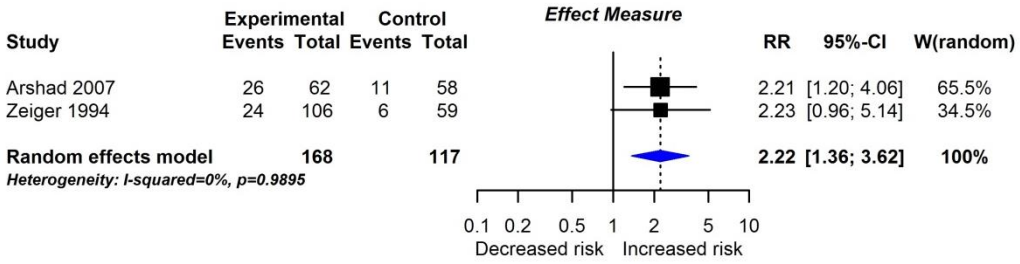


Figure 6 Early cow's milk introduction and the risk of FA-Any at age 5-14 years



Note – both studies included advice regarding timing of cow's milk introduction, but both studies also included other dietary and/or non-dietary interventions.

Figure 7 Early cow's milk introduction and risk of FA-CM at age ≤4 years

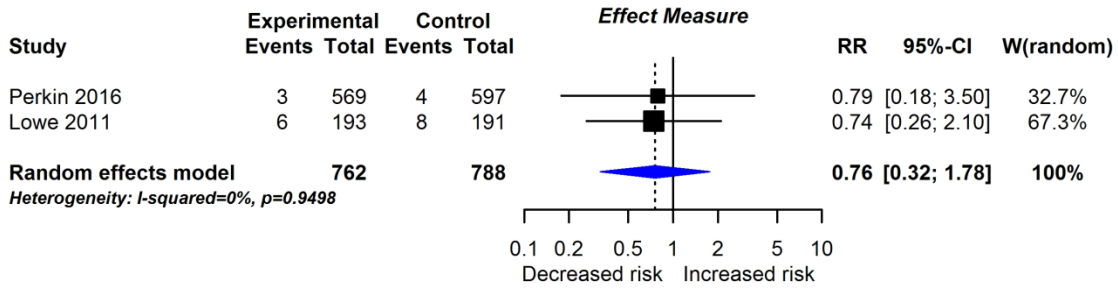
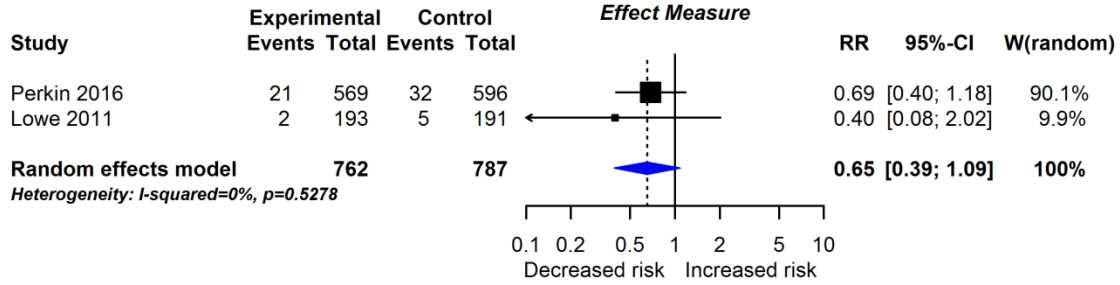


Figure 8 Early cow's milk introduction and risk of FA-Egg at age ≤4 years



2.3. Conclusions: cow's milk introduction and FA

Overall 9 studies reported this association. Although 2 multifaceted studies found evidence for increased FA-Any at age 5-14 with early cow's milk introduction, this was not supported by analysis of a larger number of studies and participants reporting FA-Any, FA-CM or FA-Egg at age 0-4.

Overall we found no evidence that early cow's milk introduction influences risk of FA.

3. Timing of soya introduction and risk of FA

Figures 9 to 13 show data from 2 studies of soya milk introduction and risk of FA. In general data are relatively sparse and do not show evidence of an association. One study of cow's milk versus soya milk formula during infancy found no significant difference in risk of FA-Any, FA-CM, FA-Egg or FA-Peanut (Lowe 2011). One multifaceted intervention study found no significant difference in risk of FA-Any at age 5-14 in the standard advice group, compared with the group advised to avoid soya for the first year (Zeiger). Zeiger separately reported food allergy in graphical form in 225 participants at age 4, which could not be included in meta-analysis. They found increased food allergy to any food in the standard advice group when using lifetime prevalence, but no significant difference when using 12-month prevalence at age 4.

Figure 9 Early soya milk introduction and risk of FA-Any at age ≤ 4 years

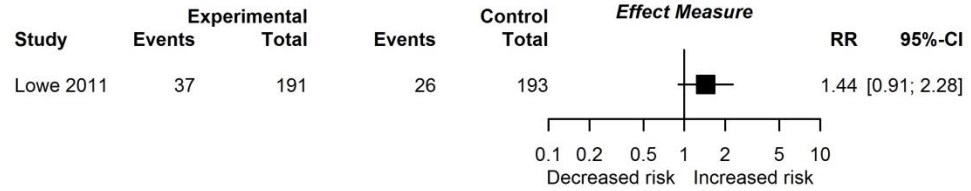
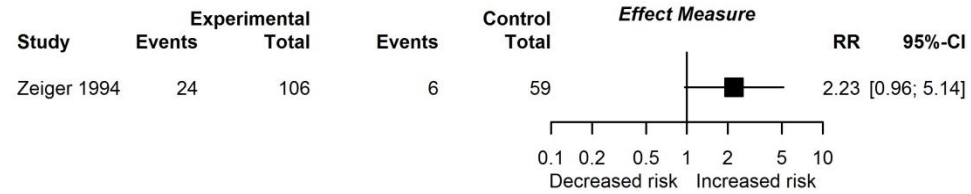


Figure 10 Early soya milk introduction and risk of FA-Any at age 5-14 years



Note – this study included advice regarding timing of cow's milk introduction, but also included other dietary interventions.

Figure 11 Early soya milk introduction and risk of FA-CM at age ≤ 4 years

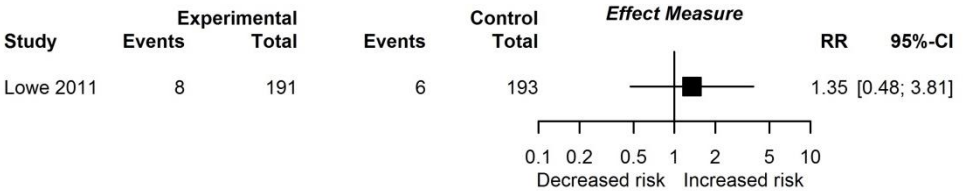


Figure 12 Early soya milk introduction and risk of FA-Egg at age ≤ 4 years

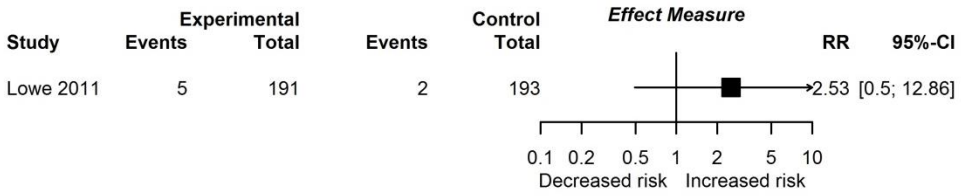
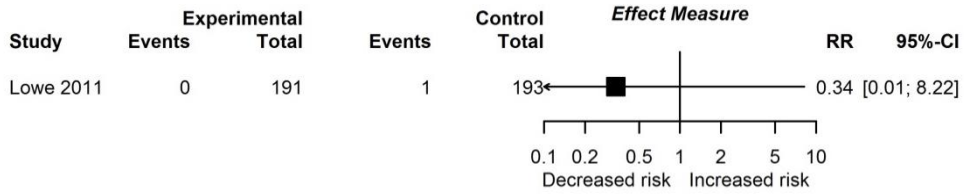


Figure 13 Early soya milk introduction and risk of FA-Peanut at age ≤ 4 years



3.1. Conclusions: soya introduction and FA

Overall 2 studies evaluated this association, and found no evidence that timing of soya introduction influences risk of FA.

Overall we found no evidence that early soya introduction influences risk of FA.

4. Timing of egg introduction and risk of FA

Figures 14 to 18 show data from studies of egg introduction and risk of FA. Data are derived from 3 studies of multifaceted interventions which included a component of delayed egg introduction; a study of early introduction of multiple foods (Perkin 2016), and 4 studies of early introduction of egg only. We found evidence that early egg introduction reduces risk of FA-Egg (Figure 17) but no evidence that early egg introduction influences risk of FA-Any (Figures 14/15) or FA-CM (Figure 16). Perkin 2016 also reported FA-Peanut, with no significant difference.

Two multifaceted intervention trials found increased risk of FA-Any at age 5-14 in participants who had unrestricted use of egg in infancy, compared with participants advised to delay introduction of egg (Figure 15). These studies have been discussed in detail in the cow's milk allergy section (Figure 6).

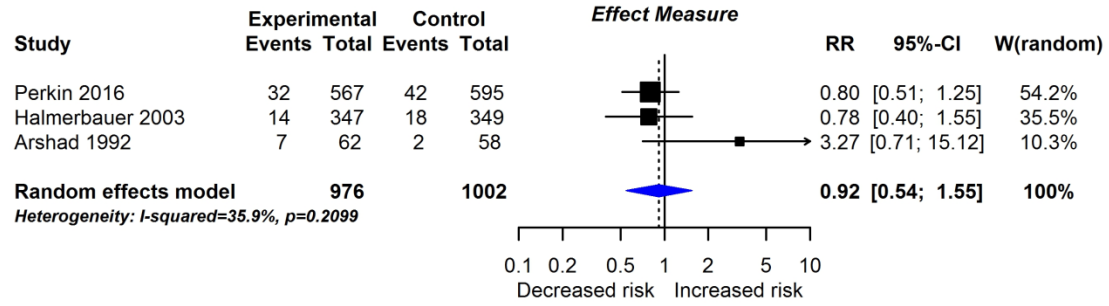
Halpern reported no significant difference in FA-Egg between infants randomised to early (9 cases) versus late (4 cases) egg introduction, but the denominators were not reported, so that we were unable to include these findings in meta-analysis.

4.1. Conclusions: egg introduction and FA

Overall 8 studies reported this outcome. We found evidence from a meta-analysis of 5 studies that early egg introduction reduces risk of egg allergy, although a sixth study which was poorly reported did not find reduced egg allergy. The level of evidence was downgraded -1 for indirectness. The reason for this is that out of the 5 studies included in meta-analysis of egg allergy, 3 studies only recruited infants without egg sensitisation ie they undertook allergy tests on infants prior to enrolment, and only included those without evidence of sensitisation to egg; 1 study only recruited infants with eczema; 1 study used multiple allergenic foods, including egg. Hence the study populations are indirect when considering a population-based intervention. We found no evidence for a relationship between timing of egg introduction and other forms of FA.

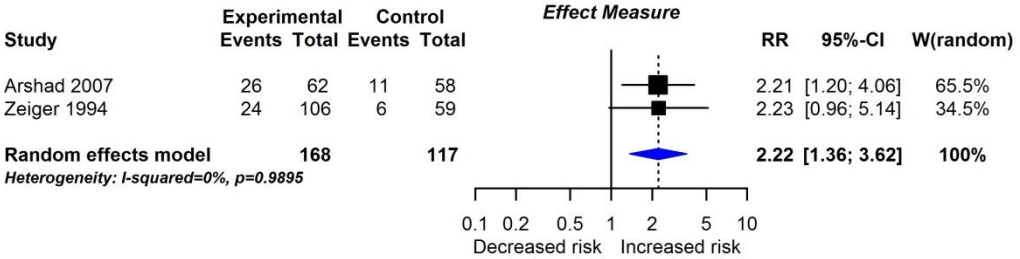
Overall we found MODERATE evidence (-1 indirectness) that egg introduction at 4-6 months reduces risk of egg allergy compared to later introduction.

Figure 14 Early egg introduction and risk of FA-Any at age ≤ 4 years



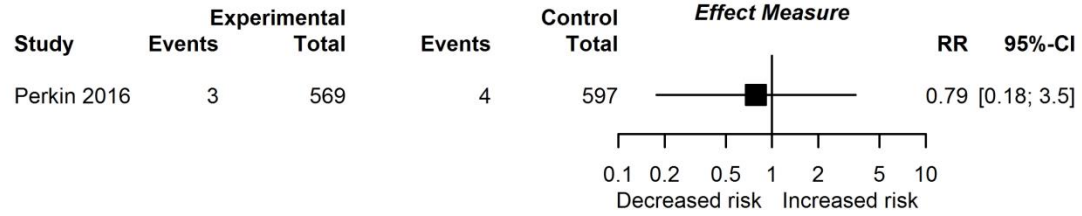
Note – studies included advice regarding timing of egg introduction, but all 3 studies also included other dietary and/or non-dietary interventions.

Figure 15 Early egg introduction and risk of FA-Any at age 5-14 years



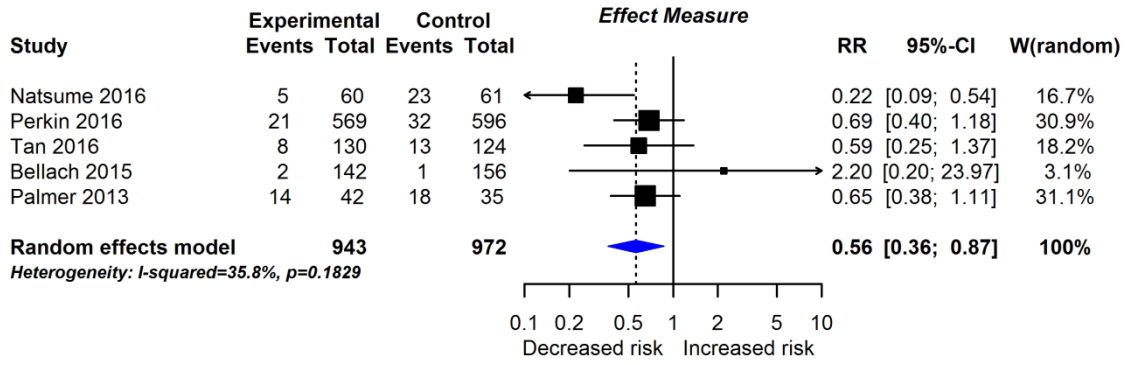
Note – both studies included advice regarding timing of egg introduction, but both studies also included other dietary and/or non-dietary interventions.

Figure 16 Early egg introduction and risk of FA-CM at age ≤ 4 years



Note – the included advice regarding timing of egg introduction, but also included other dietary interventions.

Figure 17 Early egg introduction and risk of FA-Egg at age ≤ 4 years

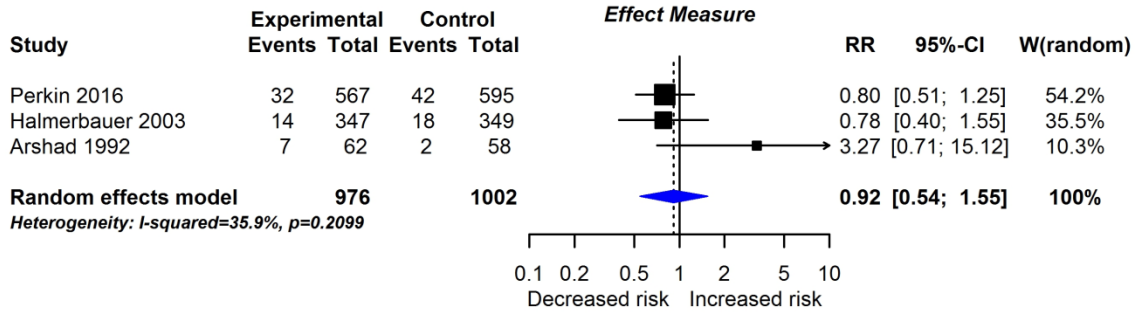


5. Timing of nut introduction and risk of FA

Figures 18 to 25 show data from studies of nut (peanut and/or tree nut) introduction and risk of FA. Data are derived from studies of multifaceted interventions which included a component of delayed peanut introduction; a study of early introduction of multiple foods (Perkin 2016), and a study of early introduction of peanut only (du Toit). We found evidence that early peanut introduction reduces risk of FA-Peanut (Figure 24) at age 5-14, but no evidence from 5 separate studies that early peanut introduction influences risk of FA-Any, FA-CM or FA-Egg. When data were combined for early peanut introduction and risk of FA-Peanut at different ages, there was evidence for an overall reduction in risk, with high statistical heterogeneity (Figure 25). This high heterogeneity may be due to differences in compliance between the intervention groups in the two studies. The study of du Toit 2015 recruited a population with established allergic disease, but without high-level sensitisation to peanut. The study of Perkin recruited infants exclusively breastfed to at least 3 months, who were otherwise broadly representative of the UK population. There was a very high level of compliance with the early peanut feeding regimen in the study of du Toit, and a more variable level of compliance in the study of Perkin 2016, where a dose response relationship between compliance and outcome (FA-Peanut) was documented.

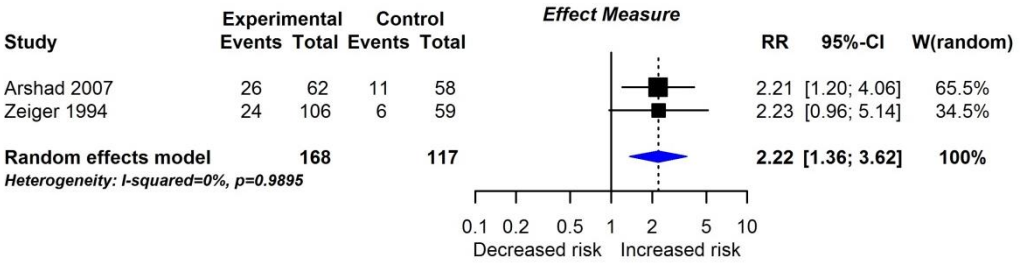
Two multifaceted intervention trials found increased risk of FA-Any at age 5-14 in participants who had unrestricted intake of nuts in infancy, compared with participants advised to delay introduction of nuts (Figure 20). These studies have been discussed in detail in the cow's milk allergy section (Figure 6).

Figure 18 Early nut introduction and risk of FA-Any at age ≤ 4 years



Note – all studies included advice regarding timing of nut introduction, but also included other dietary and/or non-dietary interventions.

Figure 19 Early nut introduction and risk of FA-Any at age 5-14 years



Note – both studies included advice regarding timing of nut introduction, but both studies also included other dietary and/or non-dietary interventions.

Figure 20 Early nut introduction and risk of FA-CM at age ≤ 4 years

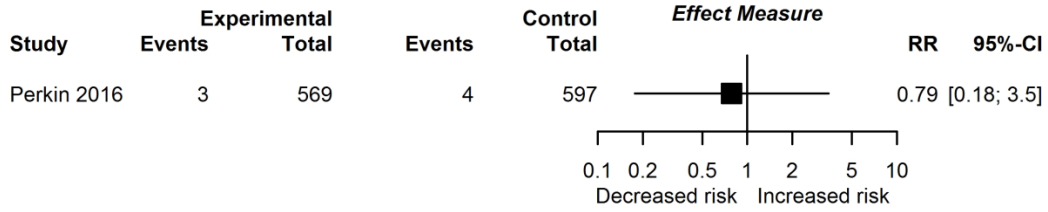


Figure 21 Early nut introduction and risk of FA-CM at age 5-14 years

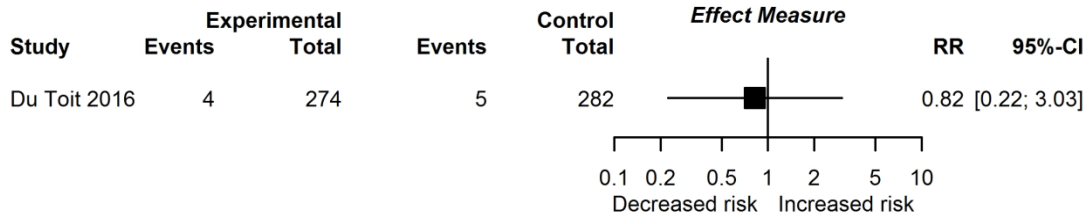


Figure 22 Early nut introduction and risk of FA-Egg at age ≤ 4 years

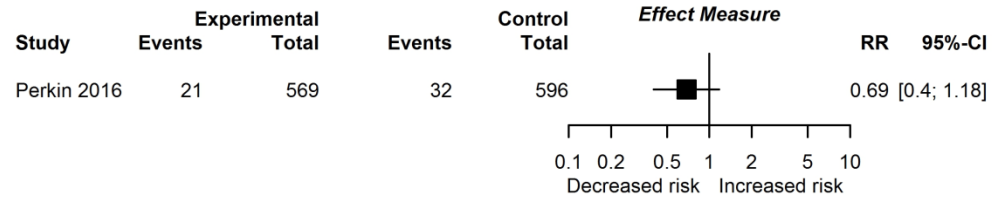


Figure 23 Early nut introduction and risk of FA-Peanut at age ≤ 4 years

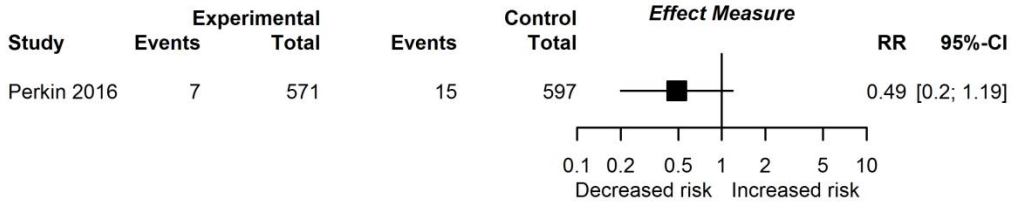


Figure 24 Early nut introduction and risk of FA-Peanut at age 5-14 years

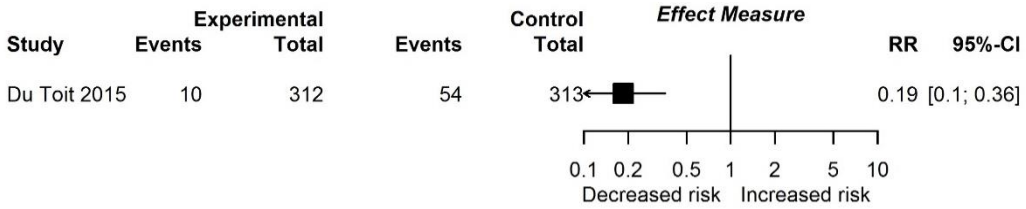
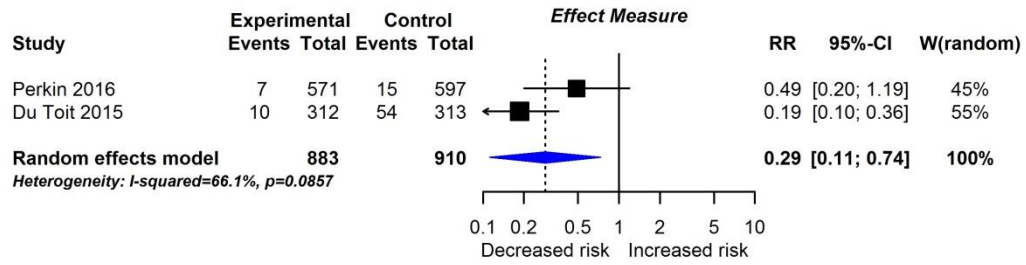


Figure 25 Early nut introduction and risk of FA-Peanut at any age



5.1. Conclusions: nut introduction and FA

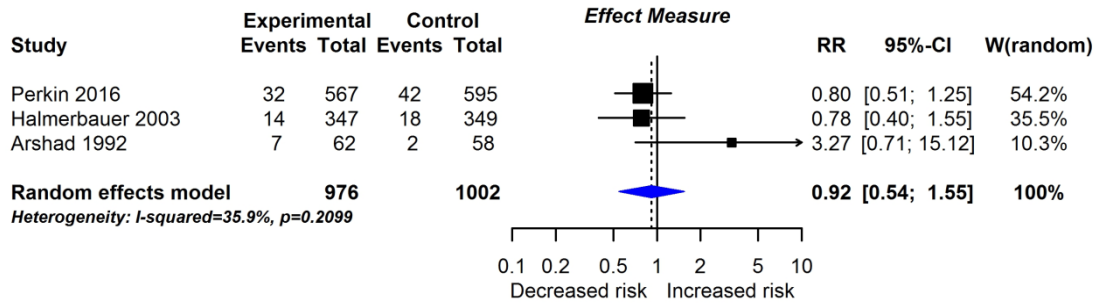
Overall 5 studies reported this association. Meta-analysis of 2 studies showed reduced FA-Peanut with early peanut introduction. Evidence was downgraded -1 for imprecision due to the wide confidence intervals; and -1 for indirectness due to the specific population studied in the trial of du Toit 2015, who had established allergic disease but no peanut sensitisation; and to the multiple interventions in the trial of Perkin 2016. Evidence was not downgraded for inconsistency, because the statistical heterogeneity is likely to be explained by differences in treatment compliance. Evidence was upgraded +1 for the strong effect size in du Toit 2015, and in pooled analysis.

Overall we found MODERATE evidence (-1 indirectness of population; -1 imprecision; +1 strong effect size) that early peanut introduction at 4-11 months reduces risk of peanut allergy compared with later peanut introduction.

6. Timing of wheat and fish introduction and risk of FA

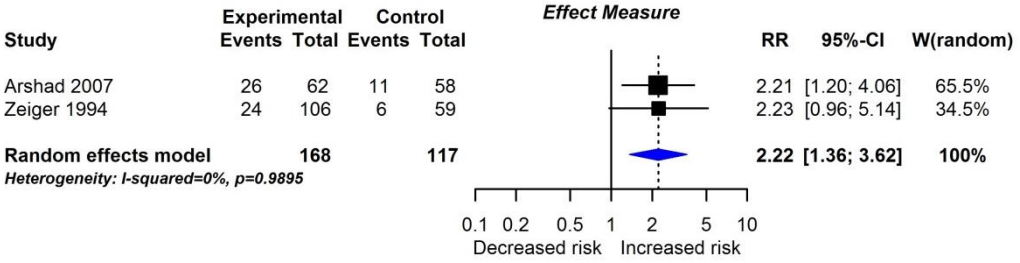
Figures 26 to 27 show data from studies of wheat and fish introduction and risk of FA. Data are derived from studies of multifaceted interventions which included a component of delayed wheat/fish introduction; and a study of early introduction of multiple foods (Perkin 2016). Two multifaceted intervention trials found increased risk of FA-Any at age 5-14 in participants who had unrestricted intake of wheat/fish in infancy, compared with participants advised to delay introduction of wheat/fish (Figure 27). These studies have been discussed in detail in the cow's milk allergy section (Figure 6). In the study of Perkin, food allergy to milk, egg and peanut did not differ significantly between early and late introduction groups, and allergy to fish was reported in just one case in the experimental arm, and one case in the control arm, between one and three years of age (P=0.97).

Figure 26 Early fish and wheat introduction and risk of FA-Any at age ≤ 4 years



Note – the studies included advice regarding fish introduction (all 3) and advice regarding wheat introduction (Perkin and Arshad) as well as studies of other dietary and/or non-dietary interventions.

Figure 27 Early fish and wheat introduction and risk of FA-Any at age 5-14 years



Note – both studies included advice regarding timing of fish and wheat introduction, but both studies also included other dietary and/or non-dietary interventions.

6.1. Conclusions: wheat and fish introduction and FA

Overall 4 studies reported this association. All studies assessed multiple interventions, so there were no direct data. There was no evidence that timing of wheat and fish introduction to the infant diet influences risk of FA.

Overall we found no evidence that timing of wheat and fish introduction influences risk of FA.

7. Timing of 'any allergenic food' introduction and risk of FA

It is possible that any effect of early allergenic food introduction is not allergen-specific. To assess evidence for this, we also undertook analysis of RCT/qRCT evidence that timing of 'any allergenic food' (AF) introduction in relation to risk of FA. These analyses were stratified by the intervention, and studies which compared early introduction of one allergenic food with another (eg cow's milk versus soya milk) were not included in these analyses (Brown 1969, Johnstone 1966, Kjellman 1979, Lowe 2011, Merrett 1988, Zhou 2014, Gruskay 1982). Figures 28 to 34 show data from studies of AF introduction and risk of FA. Findings are similar to those of previous analyses in this report, and do not contribute significant added information.

Figure 28 Early AF introduction and risk of FA-Any at age ≤ 4 years

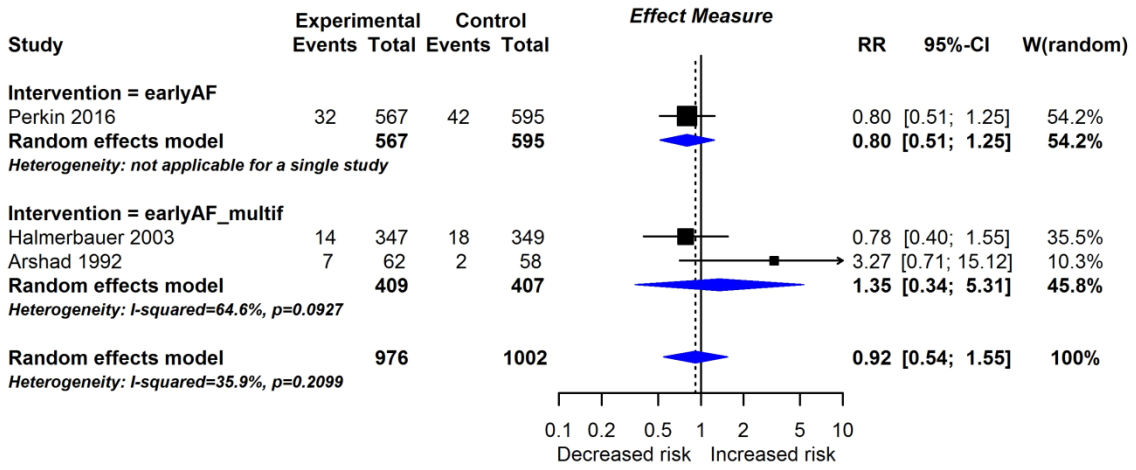


Figure 29 Early AF introduction and risk of FA-Any at age 5-14 years

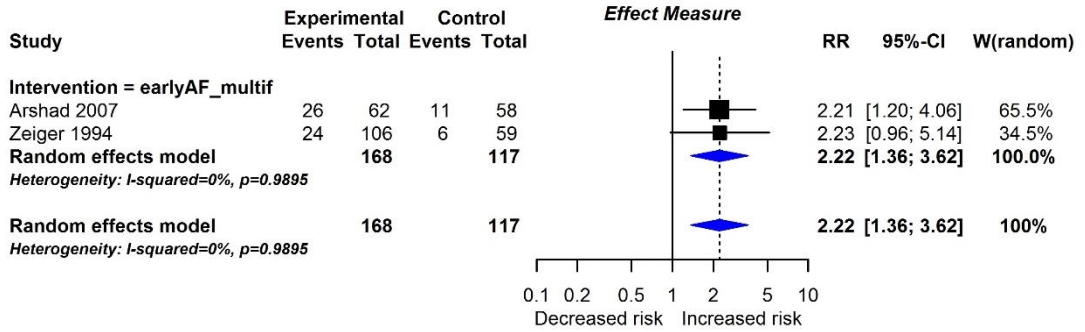


Figure 30 Early AF introduction and risk of FA-CM at age ≤4 years

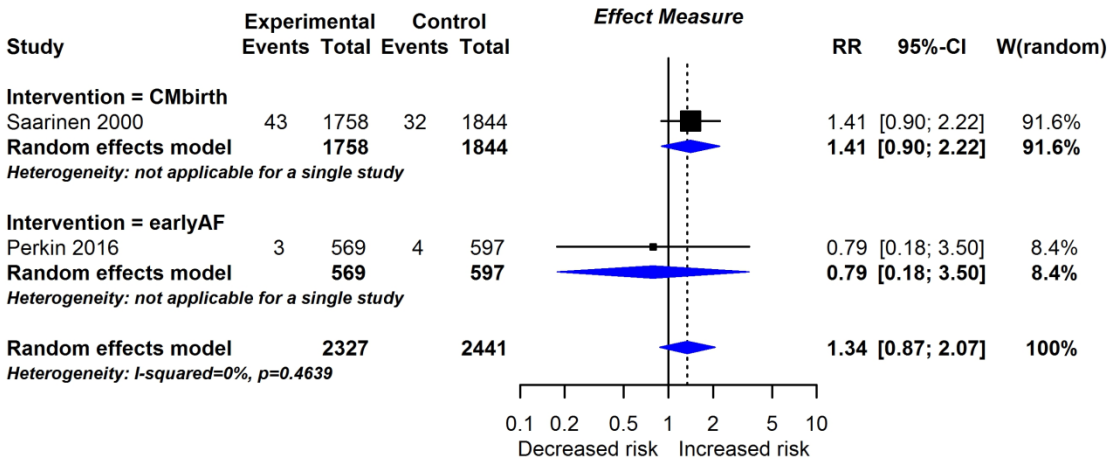


Figure 31 Early AF introduction and risk of FA-CM at age 5-14 years

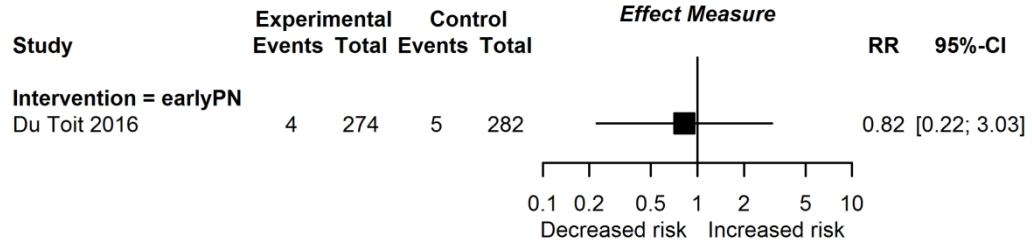


Figure 32 Early AF introduction and risk of FA-Egg at age ≤4 years

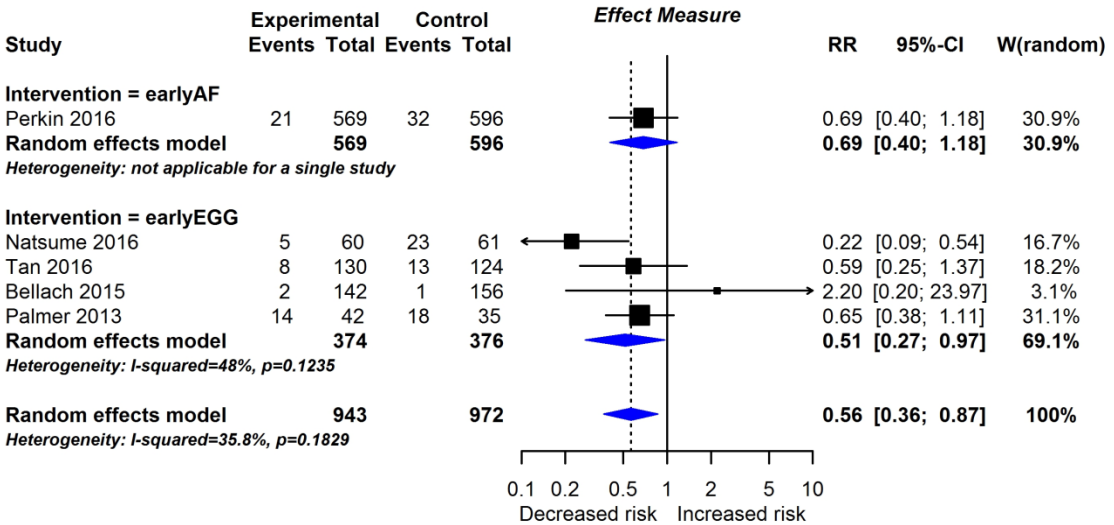


Figure 33 Early AF introduction and risk of FA-Peanut at age ≤4 years

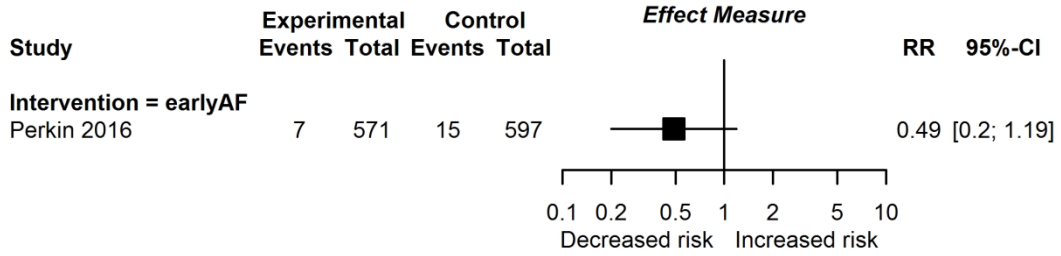
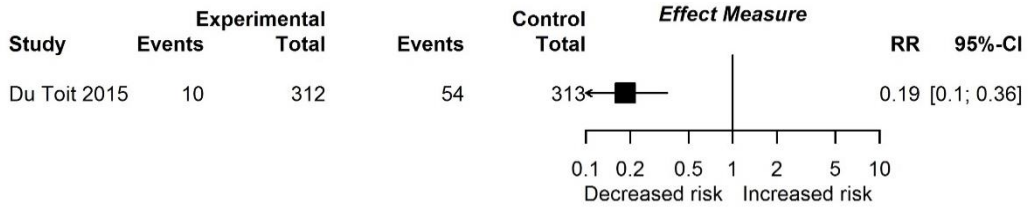


Figure 34 Early AF introduction and risk of FA-Peanut at age 5-14 years



8.1. Conclusions: any allergenic food introduction and FA

Overall 7 studies reported this outcome. There was evidence in one meta-analysis that early allergenic food introduction reduces risk of FA-Egg (Figure 36). Both trials included in this meta-analysis used early egg introduction as part or all of the study intervention. Similarly early allergenic food reduced risk of FA-Peanut at age 5-14 years, but the single study used just peanut as the intervention (Figure 34). Thus these analyses do not demonstrate non allergen-specific effects of early allergenic food introduction.

Overall we did not find evidence that early allergenic food introduction influences risk of FA in a non-allergen specific manner.

8. Timing of allergenic food introduction and risk of FA to the same food

In order to fully evaluate the possibility that timing of allergenic food introduction influences risk of FA to the same food, we meta-analysed studies where timing of allergenic food introduction was modified as part of the intervention, and the outcome FA to the intervention food(s) was reported. If the phenomenon of oral tolerance, first described in guinea pigs over 100 years ago, is relevant to humans – then one might expect a similar, allergen-specific effect across all common food allergens.

Figure 35 shows data from studies of AF introduction and risk of FA to the same food; Pooled analysis shows extreme statistical heterogeneity, largely attributable to the study of du Toit which reported more positive findings than other studies. Meta-analysis with this study excluded showed reduced, but still high, heterogeneity (RR 1.03; 95%CI 0.72, 1.49; I^2=52%).

Figure 36 shows the same data, but restricted to analysis of single foods only. There is high statistical heterogeneity, driven by the study of du Toit. Analysis of milk allergy data with the qRCT of Saarinen excluded showed no significant effect (RR 0.76; 95%CI 0.32, 1.77; I^2=0%).

The statistical heterogeneity attributable to the study of du Toit may be due to the very high rate of compliance with the treatment regimen in the study of du Toit; or to the nature of their study population who had egg allergy and/or moderate/severe eczema, and skin prick test reactivity to peanut within a predefined range.

Figure 35 Early AF introduction and risk of FA to the same food

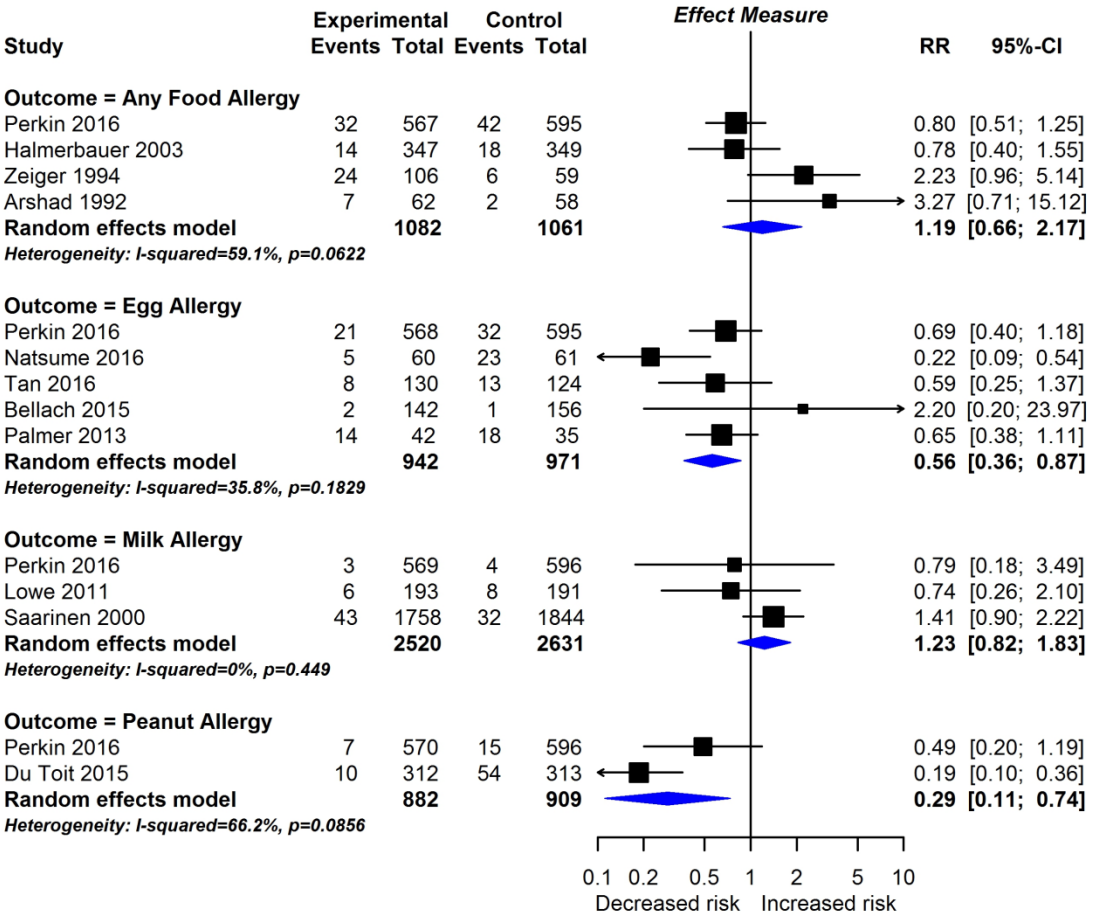
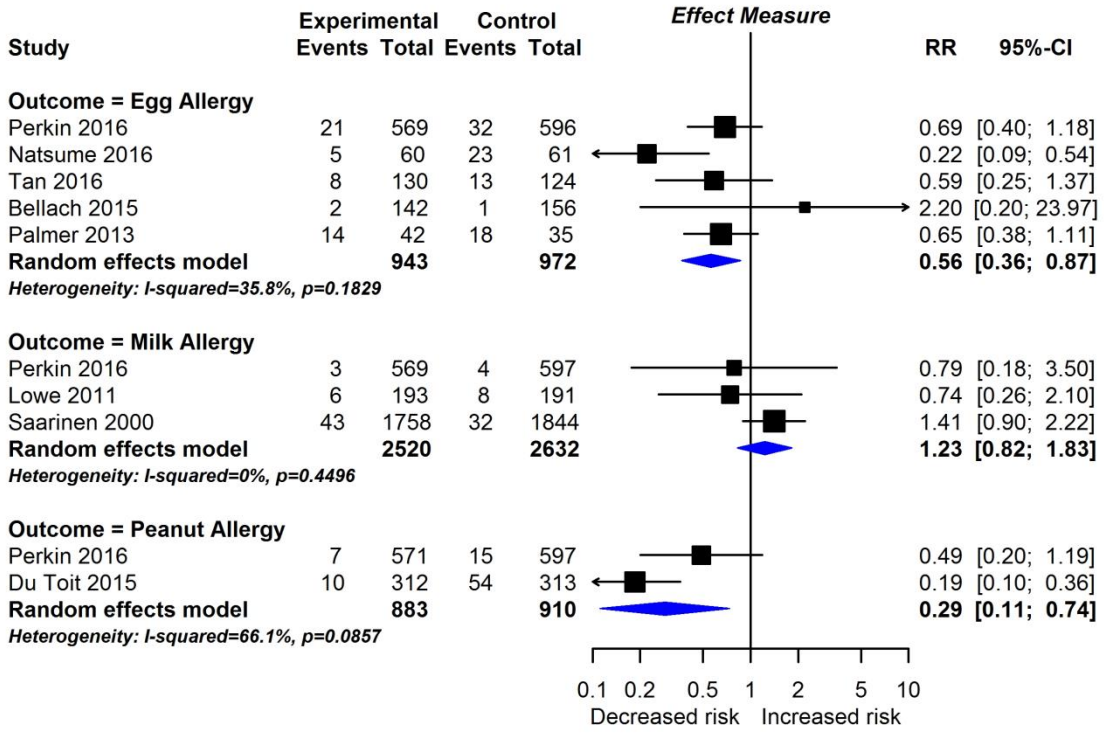


Figure 36 Early AF introduction and risk of FA to the same food (single foods only)



9.1. Conclusions: allergenic food introduction and FA to the same food

Overall 11 studies reported this association. Statistical heterogeneity was extreme or high, suggesting that the relationship between timing of allergenic food introduction and FA to the same food may not be the same for all allergenic food introduction treatment regimes or study populations.

Overall we did not find evidence that early allergenic food introduction influences risk of FA for all food allergens – in this analysis we found reduced risk of peanut allergy with early peanut introduction, reduced egg allergy with early egg introduction, but no reduced risk for milk allergy or 'any food allergy' with early introduction of the relevant food(s).

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