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EAACI food allergy prevention guidelines 2020

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Dietary prevention of food allergy

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Revision of EAACI food allergy prevention guidelines 2014

EAACI Food Allergy Prevention Task Force:

Chairs: Susanne Halken & Antonella Muraro

Coordinator: Graham Roberts

Methodologist: Debra de Silva

Other members:



Ekaterina Khaleva, Elizabeth Angier, Stefania Arasi, Hasan Arshad, Henry Bahnson, Kirsten Beyer, Robert Boyle, George du Toit, Motohiro Ebisawa, Philippe Eigenmann, Kate Grimshaw, Arne Hoest, Carla Jones, Gideon Lack, Kari Nadeau, Liam 'O'Mahony, Hania Szajewska, Carina Venter, Valérie Verhasselt, Gary Wong, Graham Roberts



Dietary prevention of food allergy

Dietary primary allergy prevention EAACI recommendations 2004, 2008 & 2014

Recommendations for all infants:

- No special diet during pregnancy or for the lactating mother
- Exclusively breastfeeding for at least 4 months

Further recommendations for high-risk infants:

If supplement is needed during the first 4 months a documented hypoallergenic formula is recommended ?

A simple and consistent message



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EAACI Food Allergy Prevention Guidelines - Revised 2020

The aim unchanged to:

- Summarize evidence about the effectiveness of approaches for the primary prevention of FA in children & adults
- Translate this evidence into Good Clinical Practice Guidelines

Differences:

- 2014: Focuses solely on studies that seek to prevent sensitization to food or FA as a primary or secondary outcomes
- 2019: Focuses solely on studies that seek to prevent FA as a primary or secondary outcomes
- 2019: GRADE



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Food Allergy and Anaphylaxis Guidelines



EAACI Food Allergy Prevention Guidelines

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From evidence to Guidelines

Received: 27 November 2019	Revised: 1 April 2020	Accepted: 5 May 2020
DOI: 10.1111/pai.13273		

ORIGINAL ARTICLE

WILEY

Preventing food allergy in infancy and childhood: Systematic review of randomised controlled trials

Debra de Silva¹ Susanne Halken² Chris Singh¹ | Antonella Muraro³ | Elizabeth Angier⁴ | Stefania Arasi⁵ | Hasan Arshad^{6,7,8} | Kirsten Beyer⁹ | Robert Boyle¹⁰ | George du Toit¹¹ | Philippe Eigenmann¹² | Kate Grimshaw^{7,13} | Arne Hoest² | Carla Jones¹⁴ | Ekaterina Khaleva¹⁵ | Gideon Lack¹¹ | Hania Szajewska¹⁶ | Carina Venter¹⁷ | Valérie Verhasselt¹⁸ | Graham Roberts^{6,8,15} | on behalf of European Academy of Allergy, Clinical Immunology Food Allergy, Anaphylaxis Guidelines Group

Pediatr Allergy Immunol. 2020;31:813-826.

Used AGREE II approach

- Stakeholder involvement
- Quality/certainty of evidence (GRADE)
- Based on the SR supplemented with expert opinions
- Identified GAPs of knowledge
- Identified benefits and harms
- Included values and preferences &
- Resource implications

Balance benefits and harms – not only a matter of efficacy



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OUH Odense Universitetshospital EAACI Food Allergy Prevention Guidelines – revision 2020 Updated protocol for systematic review and guideline Other evidence Expert opinion Updated systematic review based on **GRADE** approach Systematic review Review of all the evidence by taskforce published in PAI **EAACI** Food Allergy Formulation of recommendations **Prevention Guidelines** were available for Public / external review of recommendations feedback on the **EAACI** website June 2020 Final guideline (Halken S et al. PAI 2021)

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Systematic review & Guideline approach 2019 - 2020

- The overall certainty of evidence is assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach
- GRADE is a framework for developing and presenting summaries of evidence to support clinical practice recommendations. A summary of findings table and evidence profile is constructed for the primary outcome of new cases of FA

We strived to:

- include easily understandable and transparent tables explaining how we come from the evidence to the recommendations
- formulate the recommendations in a clear and transparent way within the GRADE recommendations



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EAACI Food Allergy Prevention Guidelines – revision 2020

Interventions – almost all dietary

Antenatal strategies

Breastfeeding mothers (+/- high risk)

Infants (+/- high risk)

- Breastfeeding
- Formulas
- Supplements (pre-, pro & synbiotics)
- Complementary foods
- Specific foods antigens

Multifacetted – dietary and environmental

Older children & adults

Many of these studies included different dietary measures e.g. hydrolysed formulas & avoidance of different solids for different periods

Food allergy defined in different ways, if defined at all

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EAACI Food Allergy Prevention Guidelines – Recommendations	OUH Odense Universitetshospital
Recommendation	Certainty of evidence
Recommendations supporting interventions	
The EAACI Task Force suggests introducing well-cooked hen's egg , but not raw egg or uncooked pasteurised raw egg, into the infant diet as part of complementary feeding to prevent egg allergy in infants	Moderate
In populations where there is a high prevalence of peanut allergy the EAACI	Allergenspecific!
Task Force suggests introducing peanuts into the infant diet in an age- appropriate form as part of complementary feeding in order to prevent peanut allergy in infants and young children	Moderate
The EAACI Task Force suggests avoiding supplementing with cow's milk formula in breastfed infants in the first week of life to prevent cow's milk allergy in infants and young obildron	Low
These are new as compared with the 2014 version	n siences
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EAACI Food Allergy Prevention Guidelines – Recommendations

Recommendation

No recommendation made

There is no recommendation for or against using **breastfeeding** to prevent food allergy in infants and young children, but breastfeeding has many benefits for infants and mothers and should be encouraged wherever possib

For infants who need a breastmilk substitute, there or against the use of regular cow's milk based in week of life to prevent food allergy

There is no recommendation for or against using p hydrolysed formula to prevent food allergy in infa When exclusive breastfeeding is not possible many substitutes are available for families to choose from, including hydrolysed formulas Halken S et al. Pediatr Allergy Immunol. 2021

In many of these studies formulas was introduced only after the age of 3-4 months, and in some even after 9 months

In most studies the diagnostic criteria for CMA was poor

Certainty of evidence



Very low

Universitetshospital EAACI Food Allergy Prevention Guidelines – Recommendations Recommendation **Certainty of evidence** No recommendation made There is no recommendation for or against vitamin supplementation or fish oil supplementation in healthy pregnant and/or breastfeeding women Very low and/or infants to prevent food allergy in infants and young children There is no recommendation for or against prebiotics, probiotics or synbiotics for pregnant and/or breastfeeding women and/or infants alone or Low in combination with other approaches to prevent food allergy in infants and young childr **Global Market Insights** PROBIOTICS MARKET probioti Market valu

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EAACI Food Allergy Prevention Guidelines – Recommendations

Recommendation	Certainty of evidence
No recommendation made	
There is no recommendation for or against using emollients as skin barriers to prevent food allergy in infants and young children	Low
There is no recommendation for or against using prophylactic oral immunotherapy to prevent food allergy in infants and young children	Low





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EAACI Food Allergy Prevention Guidelines – Recommendations

Recommendation	Certainty of evidence
Recommendations against interventions	
The EAACI Task Force suggests against restricting consumption of potential food allergens during pregnancy or breastfeeding in order to prevent food allergy in infants and young children	Very low
The EAACI Task Force suggests against introducing soy protein-based formula in the first six months of life to prevent cow's milk protein allergy in infants and young children	Very low
The EAACI Task Force suggests against using Bacillus Calmette-Guérin (BCG) vaccination to prevent food allergy in infants and young children	Low



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Dietary prevention of food allergy

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Tracy J Pitt et al. JACI 2018



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Supplementation with cow's milk formula in the first week of life

The EAACI Task Force suggests supporting breast feeding and avoid supplementing with routine cow's milk formula in breastfed infants in the first week of life to prevent cow's milk allergy in infants and young children

Reason for recommendation

Our SR included 1 trial and found that avoiding supplementation with routine CMF in the first 3 days may result in a large decrease in the risk of CMA in early childhood. WHO also warns that any supplementation may be associated with a reduction in breastfeeding

Details in Online Supplement



Supplementation with cow's milk formula in the first week of life

The EAACI Task Force suggests supporting breast feeding and avoid supplementing with cow's milk formula in breastfed infants in the first week of life to prevent cow's milk allergy in infants and young children

Strength of recommendation

This is not the strongest recommendation possible because the evidence is of low certainty. Only one trial available with multiple interventions, making it difficult to apply the findings to practice. However, the trend is supported by other studies not eligible for the review

Practical implications

Healthcare professionals and families could avoid supplementation with CMF in breast fed infants the first week. It is important to support breast feeding, which usually is sufficient with no need for supplementation in healthy, term born infants. If needed, the family should seek advice from healthcare professionals. Other possible supplementary options might include ,e.g. donor breast milk, hydrolysed formula, amino acid formula or water depending on clinical, cultural and economic factors.



EAACI Food Allergy Prevention Guidelines – Recommendations

Hydrolysed infant formula

There is no recommendation for or against using partially or extensively hydrolysed formula to prevent cow's milk allergy in infants. When exclusive breastfeeding is not possible many substitutes are available for families to choose from, including hydrolysed formulas

Reason for recommendation

Our SR included 9 trials about this. The review found that pHF or eHF hydrolysed whey or casein formula may not reduce the risk of CMA compared to conventional CM formula. There is no consistent evidence that HF reduces the risk of FA nor is there consistent evidence that HF causes harm. There was little to no evidence that one type of HF was more effective than others. The evidence is of low certainty. Trials used different formulas, introduced them at different times, often had small samples and often did not use robust diagnostic criteria for food allergy

Practical implications

Breastfeeding of all infants is preferable, but when a breastmilk substitute is needed, professionals could help families consider the best possible alternative for a family's individual circumstances. The options discussed could include a hydrolysed infant formula



Hydrolyzed formula – controversies on FA

EAACI Food Allergy Anaphylaxis Guidelines 2014 Vandenplas Yvan et al. JPGN 2014. SR Boyle RJ. BMJ 2016. SR & Meta-analysis Osborne DA. Cochrane Review 2018

Difficult to evaluate

- Many poor quality, small studies
- Outcomes varying & mixed
- Mix of different methods and populations
- Mix of different interventions and products
 - Duration of BF? Weaning?
 - Age and duration of HF?
- Varying follow-up & age for evaluation?
- Reporting of results



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Huge differences:

- in-/exclusion criteria
- publications included

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Hydrolyzed infants formula (HF) - FA

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Comparability of HF's

Any change in the formulation may change the allergenicity by e.g.

- Changing the epitopes (Conformational vs. Linear)
- Aggregation of smaller peptides
- Contamination

The allergenicity may be changed by adding e.g.

- Fatty acids: DHA and ARA
- Pre- and probiotics
- Different HF's may not be comparable despite the same classification as regards degree of hydrolysis
- Many HF's used in studies are experimental and not comparable to commercial HF's



Considerations for implementing recommendations made in this guideline

Торіс	Barriers to implementation	Facilitators to implementation
Introducing cooked egg into the infant diet	Infants may not enjoy the texture or taste until later in infancy	Knowledge about the preventive impact amongst parents and healthcare professionals
Introducing peanut into the infant diet	Families with known peanut allergy may want to refrain from introducing peanut in the home due to risk of allergic reactions in other family members. Parents may not wish to feed their infants quantities of monosaturated fat. It may be difficult to feed infants peanut butter or peanut snacks	Knowledge about the preventive impact amongst parents and healthcare professionals



Considerations for implementing recommendations made in this guideline

Торіс	Barriers to implementation	Facilitators to implementation
Avoiding temporary supplementation with cow's milk formula in the first week of life	Standard cow's milk formula has historically been used in some countries as a supplementation in the first week of life, often without reason and without parent knowledge	Knowledge about the potential deleterious impact of temporary supplementation and about alternative supplements amongst parents and healthcare professionals
Avoiding introducing raw (pasteurized) egg into the infant diet	None, except for eventual certain lifestyles, where this is normal part of infant feeding	Knowledge about potential harms amongst parents and healthcare professionals



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Key changes from the 2014 guideline include suggesting

- Supporting breast feeding & avoiding supplementation with cow's milk formula in the first week of life (low certainty of evidence)
- The introduction of peanut and well-cooked egg as part of complementary feeding (moderate certainty of evidence)
- Avoiding cow's milk formulas in the 1 week of age
- No recommendation for different infant formulas or hydrolysed cow's milk based formulas
- No evidence is not identical with no effect
- More well-powered, multinational research using robust diagnostic criteria is needed



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Dietary primary prevention of food allergy - EAACI recommendations 2020

- No special diet during pregnancy or lactation
- Exclusively breastfeeding for at least 4 months
- Avoidance of supplement with cow's milk based formula the first week of life
- If a breastmilk substitute is needed, a cow's milk based infant formula incl. hydrolysed formulas can be used
- Well-cooked, but not raw or uncooked pasteurized egg, and peanut can be introduced as part of complementary feeding, the latter in populations with high prevalence of peanut allergy

Simple recommendations which require minimal cost or resources



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EAACI Food Allergy Prevention Guidelines

Good Clinical Practice Guidelines necessary!

- Dissemination
- Implementation
- To make a difference for our patients

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There is a need for robust education & promotional campaigns to help parents, professionals, policy makers and commissioners understand the best ways to ensure a healthy & balanced diet & to reduce food allergy





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One size does not necessarily fit all!

So guidelines need to be adapted to the local, cultural and familiar conditions & ressources

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Development of cow's milk allergy – DK experiences

Early exposure to cow's milk proteins

A danish prospective study of a one year birth-cohort 1985 found:

- 88% of newborns received supplement of regular CM formula during the first 5 day at the nursery – often without their mothers knowledge
 - 40-860 ml the first 5 days: 39 / 1539 developed CMPA*
 - No formula the first 5 days: 0 / 210 developed CMPA*

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• 40 ml CM formula ~ 0.4 g BLG~ 8000 l Human milk

Høst A et al. Acta Paediatr Scand 1988;77:663-70*



Dietary prevention of food allergy in Denmark until now

Dietary primary allergy prevention in DK from 1988

Recommendations for all infants:

- No special diet during pregnancy or for the lactating mother
- Exclusively breastfeeding for at least 4 months

Further recommendations for high-risk infants:

• If supplement is needed during the first 4 months a documented hypoallergenic formula is recommended ?

EAACI recommendations 2004, 2008 & 2014



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Food Allergy and CMPA in two comparable unselected birth cohorts in Odense, 14 years apart, in children 0-18 months

	Cumulated prevalence	
	1985 (n 1749)	1999 (n 495)
Food allergy	7.4% (6.2-8.6)	3.4% (1.8-5.0)
Cow's milk protein allergy	2.2% (1.5-2.9)	0.9% (0.1-1.7)
1988 the present prevention program* was 1 introduced		

* EAACI 2014



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Reviderede anbefalinger om forebyggelse af fødevareallergi hos spædbørn

Sundhedsstyrelsen 08.06.2022





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Reviderede anbefalinger om forebyggelse af fødevareallergi hos spædbørn ^{Odense} Sundhedsstyrelsen 08.06.2022

Amning

Amning anbefales på grund af positive helbredskonsekvenser for mor og barn

> Ikke evidens for at amning beskytter mod fødevareallergi

Modermælkserstatning i første leveuge

Undgå supplement med alm. komælksbaseret ME til børn der ammes

- Børn med behov for ME anbefales højt hydrolyseret eller aminobaseret modermælkserstatning den første leveuge – uanset allergidisposition
- Spædbørn indlagt på neonatalafdeling ernæres efter afdelingens retningslinjer og en individual vurdering i henhold til barnets samlede tilstand og behov



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Reviderede anbefalinger om forebyggelse af fødevareallergi hos spædbørn Sundhedsstyrelsen 08.06.2022

Modermælkserstatning fra 2. leveuge

- Efter 1. leveuge og I første leveår kan anvendes alm. Eller hydrolyseret komælksbaseret ME til spædbørn, som har brug for modermælkserstatning
- Ikke fundet evidens for hverken at anbefale eller fraråde alm eller hydrolyseret komælksbaseret ME for at forebygge fødevareallergi
- Forældrenes valg af ME de første 4 mdr., ved behov herfor, må bero på en afvejning af fordele og ulemper, familiens ønsker og evt. bekymring for allergi.

Soyaproteinbaseret modermælkserstatning

Der er ikke evidens for at soyaproteinbaseret modermælkserstatning forbygger udvikling af mælkeallergi

Kan evt. anvendes ved ønske om vegansk ernæring, galactosæmi mm



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Overgangskost

Ingen restriktioner vedr. Overgangskost mhp forebyggelse af fødevareallergi

- > Alle fødevarer kan gradvist introduceres fra 4-6 mdr. i alderssvarende form
- Der er nogen evidens for at man kan reducere risikoen for ægallergi ved at introducere hårdkogt æg som fast bestanddel af kosten et par gange ugentligt som del af overgangskosten

Moderens kost

Gravide og ammende anbefales sund og varieret kost jvf officielle kostråd

- > Potentielle allergifremkaldene fødevarer bør ikke fravælges
- Udelukkelse af hele fødevaregrupper kan medføre mindsket indtag af vigtige næringstoffer og have negative helbreds effekter på mor og barn



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- Ingen særlig diæt/tilskud til mor under graviditet eller amning
- Så vidt muligt udelukkende amning mindst de første 4 mdr
- Undgå supplement med alm. komælksbaseret ME den første leveuge
 - Obs barselsafdeling og neonatalafdeling
- Hvis modermælkserstatning er nødvendig, kan alm. ME ofte anvendes. Ved særligt behov, f.eks. udtalt allergidisposition/ bekymring for fødevareallergi kan hydrolysede produkter de første levemdr. overvejes
- Alm. varieret overgangskost, inkl. velkogt æg i aldersvarende form, kan introduceres når barnet er klar fra 4-6 mdrs alderen

Børn med symptomer på fødevareallergi bør vurderes med henblik herpå!



Food Allergy Prevention Guidelines Translating knowledge for best practice in healthcare

Optimal intervention Safet Sufficient

Optimal quality of life

One size does not necessarily fit all



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